

आहार वितरण विवरणी -

श्री साता

सामान्य 7-3

Guide to

INTRODUCING

HPV VACCINE

INTO NATIONAL  
IMMUNIZATION  
PROGRAMMES

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Guide to

INTRODUCING

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**HPV VACCINE**

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INTO NATIONAL  
IMMUNIZATION  
PROGRAMMES





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## ABBREVIATIONS

<b>AD syringe</b>	Auto-disable syringe
<b>AEFI</b>	Adverse event following immunization
<b>cMYP</b>	Comprehensive multi-year plan
<b>CTC</b>	Controlled Temperature Chain
<b>EPI</b>	Expanded Programme on Immunization
<b>EVM</b>	Effective vaccine management
<b>GACVS</b>	Global Advisory Committee on Vaccine Safety
<b>HIV</b>	Human immunodeficiency virus
<b>HPV</b>	Human papillomavirus
<b>IARC</b>	International Agency for Research on Cancer
<b>ICC</b>	Inter-agency coordinating committee
<b>IEC</b>	Information, education and communication
<b>MOH</b>	Ministry of Health
<b>NITAG</b>	National immunization technical advisory group
<b>SAGE</b>	Strategic advisory group of experts on immunization
<b>UNESCO</b>	United Nations Education, Scientific and Cultural Organization
<b>UNFPA</b>	United Nations Population Fund
<b>UNICEF</b>	United Nations Children's Fund
<b>VLP</b>	Virus-like particle
<b>VVM</b>	Vaccine vial monitor
<b>WHO</b>	World Health Organization





## ABOUT THIS GUIDE

This document is intended for use by national immunization programme managers and immunization partners involved in providing implementation support to countries.

General guidance about planning the introduction of a vaccine into a national immunization programme is provided in the document *Principles and considerations for adding a vaccine to a national immunization programme: from decision to implementation and monitoring* published by the World Health Organization (WHO) in 2014 and available at [http://www.who.int/immunization/programmes\\_systems/policies\\_strategies/vaccine\\_intro\\_resources/nvi\\_guidelines/en/](http://www.who.int/immunization/programmes_systems/policies_strategies/vaccine_intro_resources/nvi_guidelines/en/).

The specific objectives of this guide are:

- To inform the policy discussions and operational aspects for the introduction of HPV vaccine into a national immunization programme.
- To provide up-to-date references on the global policy, as well as the technical and strategic issues related to the introduction of HPV vaccine into a national immunization programme.

Globally, there is almost a decade of HPV vaccine introduction experience from dozens of countries across all income groups. WHO has compiled these lessons and their implications for action in a companion document entitled *Scaling Up HPV Vaccine Introduction* published in 2016 and available at: <http://www.who.int/immunization/diseases/hpv/scaling-up-intro/en/>



# 1. INTRODUCTION

## HPV INFECTION AND CERVICAL CANCER

Cervical cancer is caused by the human papillomavirus (HPV). More than 100 HPV types have been identified to date, about 40 of which can infect the genital area. Two high-risk types of HPV, types 16 and 18, account for about 70% of all cervical cancer cases. HPV can also cause other types of anogenital cancer (vagina, vulva, anus, penis), head and neck cancers, and genital warts in both men and women.

Immunodeficiency is the strongest known cofactor for HPV in cervical and anal cancers.<sup>1</sup> In people living with HIV compared to people who are not, HPV infections are more likely to occur, persist, and progress to cancer.

HPV is sexually transmitted and most people become infected sometime during their lifetime, usually soon after becoming sexually active. Most infections are asymptomatic and usually clear up without any intervention within a few months, and about 90% clear within two years. A small proportion of infections with certain types of HPV can persist and progress to cancer. If infection from cancer-causing HPV types persists over a long period of time, women can go on to develop precancerous lesions that, if left untreated, develop into cervical cancer. This process takes on average 20–30 years from infection to development of cervical cancer.

Although it is preventable, according to the most recent data available (IARC GLOBOCAN 2012<sup>2</sup>), cervical cancer is the fourth most common cancer among women worldwide. It is estimated that each year there are approximately 528,000 new cases and more than 266,000 deaths from cervical cancer. More than 85% of all new cases and deaths occur in less developed countries, partly because routine cervical cancer screening and treatment are not widely available.

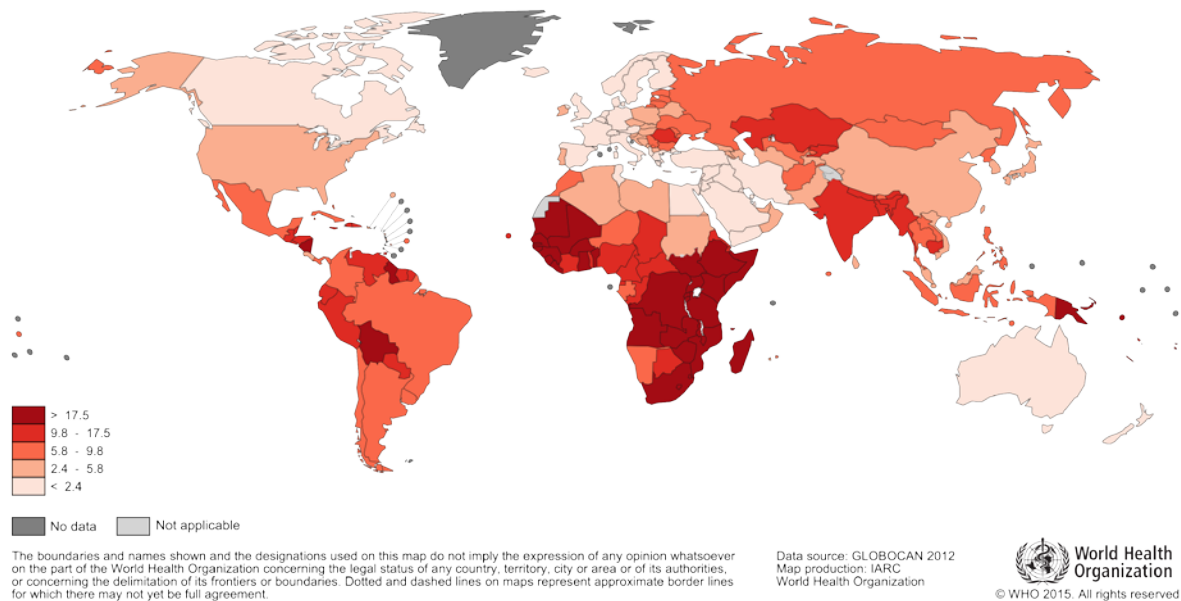
Regions with the highest risk include Eastern Africa, Melanesia, Southern and Central Africa (**Figure 1**). Unless cervical cancer prevention and control measures are successfully implemented, it is estimated that by 2030, approximately 800,000 new cases of cervical cancer will be annually diagnosed. The vast majority of these cases will be in developing countries.

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<sup>1</sup> Denny LA, Franceschi S, de Sanjosé S, et al. Human papillomavirus, human immunodeficiency virus and immunosuppression. *Vaccine* 2012, 30 Suppl 5:F168–174.

<sup>2</sup> International Agency for Research on Cancer (IARC), GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012. [http://globocan.iarc.fr/Pages/fact\\_sheets\\_cancer.aspx](http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx)

Figure 1. Cervical cancer age-standardized mortality rates (ASR) by country, 2012



## HPV VACCINATION: PART OF A COMPREHENSIVE APPROACH TO PREVENTION OF CERVICAL CANCER

**Cervical cancer  
can be prevented**

Since 2009, WHO has recommended the inclusion of HPV vaccination into national immunization programmes in countries where cervical cancer is a public health priority and where cost-effective and sustainable implementation of the vaccine is feasible.<sup>3</sup>

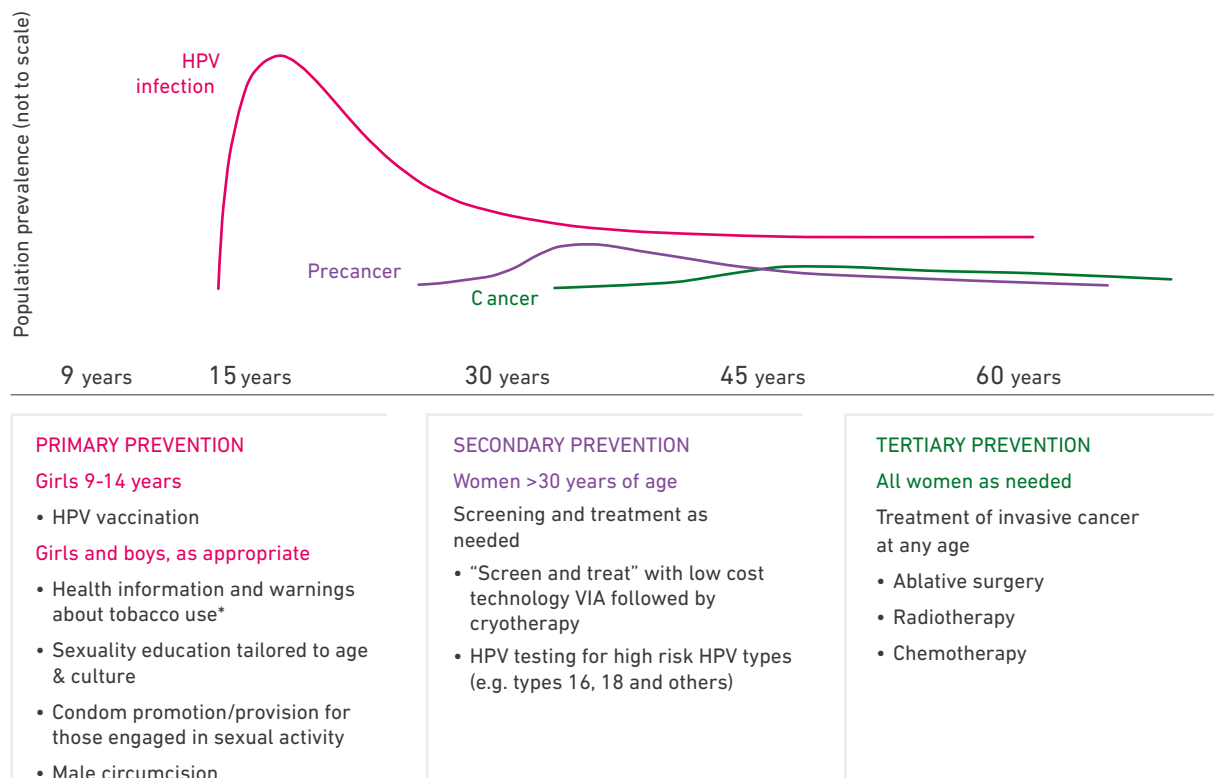
Because HPV vaccines do not protect against all HPV types that cause cervical cancer, vaccine introduction should be part of a coordinated and comprehensive approach to cervical cancer control (Figure 2) that includes:

- Prevention primarily through vaccination of 9-14 year old girls prior to exposure and acquisition of HPV infection;
- Secondary prevention through screening and treatment of adult women for pre-cancerous lesions, and
- Tertiary and palliative care for women affected by cervical cancer.

HPV vaccine introduction should not be deferred in countries where the other relevant interventions are not available. On the contrary, the introduction of HPV vaccine can provide an important strategic opportunity for improving or establishing cervical cancer screening and treatment programmes, and raising awareness of their purpose and availability.

<sup>3</sup> <http://www.who.int/immunization/documents/positionpapers/en/>

Figure 2. Programmatic interventions to prevent HPV infections and cervical cancer



\* Tobacco use is an additional risk factor for cervical cancer.

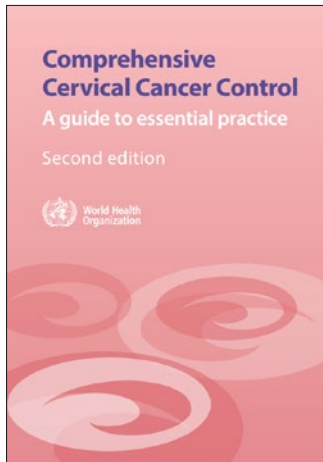
### A CHECKLIST FOR A COMPREHENSIVE CERVICAL CANCER PREVENTION AND CONTROL PROGRAMME

1	A functional multi-disciplinary platform to foster partnership and collaboration and set the national agenda	✓
2	A comprehensive national policy or plan on cervical cancer prevention and control	✓
3	National guidelines for health workers for all components of comprehensive cervical cancer prevention and control	✓
4	Financial and technical resources to implement the policy/plan and ensure that services are accessible and affordable to girls and women	✓
5	Communication strategies to educate the community and advocate for support of national policies	✓
6	A training plan in place, as well as supervisory mechanisms for quality control and assurance of the programme	✓
7	HPV vaccination as a population based strategy to an appropriate cohort in the target age group of 9 and 14 year old girls	✓
8	Cervical cancer programme to 'screen and treat' every women between 30 and 49 years old at least once in her life time	✓
9	A functioning referral system that links screening services with the treatment of precancerous lesions and invasive cancer	✓
10	Functioning monitoring systems to track coverage of HPV vaccination, screening and follow-up treatment	✓
11	Existence of a cancer registry as part of the health information system to monitor cervical cancer incidence and mortality	✓

Adapted from: *Comprehensive cervical cancer prevention and control - WHO guidance, March 2013.*



### KEY RESOURCES – Comprehensive Approaches



<http://www.who.int/reproductivehealth/publications/cancers/cervical-cancer-guide/en/>



<http://www.who.int/reproductivehealth/publications/cancers/9789241505147/en/>

## HPV VACCINES

Currently licensed HPV vaccines prevent cervical cancer by preventing infection by various HPV types. The vaccines are most effective when administered to a person prior to exposure to HPV; the vaccines are not therapeutic and cannot be used for treatment of cervical cancer or HPV infection.

Two HPV vaccines are currently pre-qualified<sup>4</sup> by WHO:

1. A bivalent vaccine (Cervarix<sup>®</sup>, produced by GlaxoSmithKline) – protects against two HPV types 16 and 18 that cause the majority of cervical cancers; and
2. A quadrivalent vaccine (GARDASIL<sup>®</sup>/Silgard<sup>®</sup>, produced by Merck & Co<sup>5</sup>.) – protects against HPV types 16 and 18, as well as HPV 6 and 11 that are responsible for anogenital warts.

As of December 2014, the U.S. Food and Drug Administration (FDA) approved Merck's 9-valent HPV vaccine (GARDASIL 9<sup>®</sup>) which includes the additional five HPV types 31, 33, 45, 52 and 58 compared to the quadrivalent vaccine. The 9-valent vaccine is currently undergoing WHO review for prequalification.

In females, the 9-valent vaccine is licensed for prevention of cervical, vulvar, vaginal, and anal cancers caused by HPV types 16, 18, 31, 33, 45, 52 and 58, pre-cancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, and genital warts caused by HPV types 6 and 11.

For the 9-valent HPV vaccine, WHO is currently coordinating a review and assessment of the incremental effectiveness (additional preventable disease burden) and cost-effectiveness for

<sup>4</sup> WHO provides a service to UNICEF and other UN agencies that purchase vaccines, to determine the acceptability, in principle, of vaccines from different sources for supply to these agencies. The detailed procedure and most recent list of prequalified vaccines can be found at: [http://www.who.int/immunization\\_standards/vaccine\\_quality/pq\\_system/en/](http://www.who.int/immunization_standards/vaccine_quality/pq_system/en/)

<sup>5</sup> Outside of the U.S.A. Merck is known as MSD Merck Sharp & Dohme.



cervical cancer prevention of immunization with the five additional HPV types, in particular in low- and middle-income countries (LMIC). This review will be complemented with modelling efforts led by independent experts.

**Table 1. Summary of HPV vaccine characteristics**

ATTRIBUTES	BIVALENT (CERVARIX®)	QUADRIVALENT (GARDASIL®/SILGARD®)	9-VALENT (GARDASIL 9®)
Vaccine type	Recombinant L1-capsid virus-like particles (VLP)	Recombinant L1-capsid virus-like particles (VLP)	Recombinant L1-capsid virus-like particles (VLP)
HPV types in vaccine	16,18	6,11,16,18	6,11,16,18 31,33,45,52,58
Disease protection	Cervical cancer (and premalignant genital lesions of cervix, vulva and vagina)	Cervical cancer (and premalignant genital lesions of cervix, vulva and vagina) Genital warts	Cervical cancer (and premalignant genital lesions of cervix, vulva and vagina) Genital warts
Cross-protection against HPV-types	31, 33	31, 45	Not necessary <sup>a</sup>
Number of doses required	2	2	2
Dosing interval (flexibility)	0 and 6 months (No maximum interval but suggested not more than 12-15 months)	0 and 6 months (No maximum interval but suggested not more than 12-15 months)	0 and 6 months (No maximum interval but suggested not more than 12-15 months)
Method of administration	Intramuscular injection	Intramuscular injection	Intramuscular injection
Presentation and Type of Vaccine Vial Monitor (VVM)	1-dose vial; VVM 30 2-dose vial; VVM 30	1-dose vial; VVM 30	1-dose vial; VVM TBD
Shelf-life	48 months at 2-8 °C for 1-dose vial; 36 months at 2-8 °C for 2-dose vial; vaccine is freeze sensitive	36 months at 2-8 °C, vaccine is freeze sensitive	36 months at 2-8 °C, vaccine is freeze sensitive
Contraindications	<ul style="list-style-type: none"> <li>• Severe allergic reaction to any vaccine component after first dose</li> <li>• Severe febrile illness</li> <li>• Known to be pregnant<sup>b</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Severe allergic reaction to any vaccine component after first dose</li> <li>• Severe febrile illness</li> <li>• Known to be pregnant<sup>b</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Severe allergic reaction to any vaccine component after first dose</li> <li>• Severe febrile illness</li> <li>• Known to be pregnant<sup>b</sup></li> </ul>

<sup>a</sup> Immunity is based on the actual VLP L1 antigen, so cross protection is unnecessary. Actual VLP antigen produces a much stronger and longer lasting immunogenic response than anything that cross protection might produce.

<sup>b</sup> Inadvertent vaccination is no reason to terminate pregnancy.

Additional information on the different HPV vaccines is available on the WHO website at [http://www.who.int/immunization\\_standards/vaccine\\_quality/PQ\\_vaccine\\_list\\_en/en/index.html](http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/index.html)

Under special conditions, some HPV vaccine products are licenced for Controlled Temperature Chain (CTC) which permits the vaccine to be kept at ambient temperatures not exceeding 40°C for up to 72 hours (See **Box 1**).



### Box 1. Controlled Temperature Chain (CTC) – beyond the traditional cold chain

The “controlled temperature chain” (CTC) is an innovative approach to vaccine management allowing vaccines to be kept at temperatures outside of the traditional cold chain of +2°C to +8°C for a limited period of time under monitored and controlled conditions, as appropriate to the stability of the antigen. A CTC typically involves a single excursion of the vaccine into ambient temperatures not exceeding +40°C and for duration of a specific number of days, just prior to administration.

WHO has established the following programmatic criteria for a vaccine to be labelled for and used in a CTC:

1. The vaccine should be used in a campaign or special strategy setting. CTC is not currently recommended for immunization through routine delivery.
2. The vaccine must be able to tolerate ambient temperatures of at least +40°C for a minimum of three days and should be accompanied by:
  - a. a vaccine vial monitor (VVM) on each vial, and
  - b. a peak threshold indicator in each vaccine carrier.
3. The vaccine must be licensed for use in a CTC by the relevant regulatory authorities, with a label that specifies the conditions.

For more information refer to the CTC website at: [http://www.who.int/immunization/programmes\\_systems/supply\\_chain/ctc/en/](http://www.who.int/immunization/programmes_systems/supply_chain/ctc/en/)

## HPV VACCINATION: SOMETHING NEW AND DIFFERENT FOR IMMUNIZATION PROGRAMMES

For many countries, the introduction of HPV vaccine into the national immunization programme is different and considerably more complicated than adding a new infant vaccine. HPV vaccination has a number of special considerations that offer both challenges and opportunities for immunization programmes.

### CHALLENGES:

- No existing **service delivery platform** (or immunization contacts) to access a new target population of 9-14 year old girls. While programmes may have experience reaching this age group with one-time, one-shot vaccination campaigns (e.g. for measles-rubella, yellow fever, meningitis A), the HPV vaccine has a 2-dose schedule.
- **Sensitivities** around HPV vaccination providing protection against a sexually transmitted infection (STI), offered for girls-only, and recurrent concerns about Adverse Events Following Immunization (AEFIs) and vaccine safety -- despite a solid safety record.
- Requires robust **communication and social mobilization** to assist with acceptance, ensure completion of schedule, and to decrease costs related to tracking drop-outs. Additionally, preparedness for crisis communication is essential.
- A uniquely **high profile vaccine** for many countries, with a broad array of stakeholders (other recent new vaccines have not had this variety, complexity, or prominence of partners).

Immunization programmes need to be prepared for HPV vaccination to be championed and/or led by others (who may not be very familiar with immunization).

- **Complex coordination and communication** among many stakeholders (to make decisions, plan, and implement). To be inclusive, new structures and mechanisms often need to be established.
- **Cost** – Not only is HPV vaccine a relatively expensive vaccine to procure, but also the operational costs of vaccine delivery are substantial (depending on the strategy, HPV vaccine delivery costs can be considerably higher than for new infant vaccines).
- **New technical or programmatic issues** such as learning how to properly locate the target population and calculate its accurate size and denominator; adopting new coverage monitoring methods; introducing informed consent processes; dealing with adolescent concerns; etc.

#### OPPORTUNITIES:

- **Demonstrating country commitment and progress on Global Action Plans** -- such as the *Global Vaccine Action Plan (GVAP) 2011-2020*<sup>6</sup> and the *Global Action Plan for the Prevention and Control of Non-Communicable Diseases (NCDs) 2013-2020*<sup>7</sup>.
- **Supporting a comprehensive approach to prevention and control of cervical cancer** because HPV vaccination does not protect against all types of HPV and cervical screening programmes will therefore still be needed, particularly for older woman who were not able to benefit from vaccination.
- **Integration** of HPV vaccination with the delivery of other health services for 9-14 year old children, provides opportunities to establish primary care for new age group of children **and health system strengthening**.
- **Broadening of stakeholders and partners** for immunization, including those from reproductive health, adolescent health, school health, cancer control, HIV prevention, and women's health.
- Vigorous **new energy and new advocacy** from the various collaborators can create synergies, innovative ways of working, new linkages, broader access, and additional resource mobilization and support for immunization.

Global experience with national HPV vaccine delivery in low and middle income countries is rapidly increasing. Countries are piloting and others adapt their approaches after national introduction. Best practices and learning have been compiled and shared. As with the management of any good programme, the introduction of HPV vaccination will require innovation, openness and flexibility to change, and a commitment to continuous quality improvement processes.

Based on current experience we know that the introduction of HPV vaccination requires substantial and prolonged hard work, strong political will, and adequate financial resources.

<sup>6</sup> [http://www.who.int/immunization/global\\_vaccine\\_action\\_plan/en/](http://www.who.int/immunization/global_vaccine_action_plan/en/)

<sup>7</sup> [http://www.who.int/nmh/events/ncd\\_action\\_plan/en/](http://www.who.int/nmh/events/ncd_action_plan/en/)

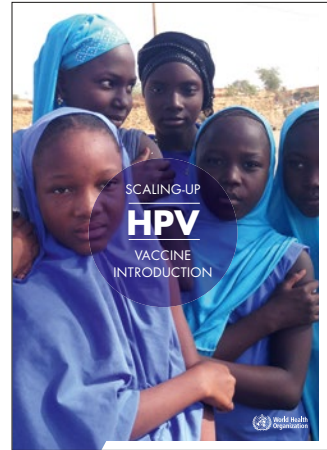


**KEY RESOURCES**

***Scaling Up HPV Vaccine Introduction***

(<http://www.who.int/immunization/diseases/hpv/scaling-up-intro/en/>)

This report summarizes key lessons and their implications for action as countries introduce and scale-up HPV vaccination as part of a comprehensive effort to reduce cervical cancer disease and death. Drawing on the *Global Learning Meeting on HPV Vaccine Introduction* held in November 2015, this report complements other efforts to compile experiences, such as the PATH/ London School of Hygiene and Tropical Medicine (LSHTM) 2015 Lessons Learnt project\*.



Specifically, this report offers experiences – many directly reported by country health managers - in the main areas of vaccine introduction: decision-making, planning and coordination, delivery strategies, communication, crises management, monitoring and evaluation, costing and sustainability. This report also offers insights into reaching hard-to-reach populations and on integration of HPV vaccine in both a comprehensive cervical cancer prevention and control plan and into adolescent health programming.

\* <http://www.rho.org/HPVlessons/index.htm>

***HPV Vaccine Introduction Clearinghouse***

(<http://www.who.int/immunization/hpv/en/>)

The **HPV Vaccine Introduction Clearing House** is a unique space to find WHO publications, tools and other important resources on the human papillomavirus vaccine (HPV).

Its purpose is to help guide HPV vaccine policy, programme and communications managers in the development of successful strategies for the introduction and sustained delivery of HPV vaccination at a national level.

The clearinghouse's 5 areas are:



# WHO RECOMMENDATIONS FOR HPV VACCINATION

Human papillomavirus vaccines: WHO position paper – October 2014<sup>8</sup>

WHO will be revising its HPV Vaccine Position Paper in 2017, in light of the SAGE October 2016 recommendations. The main changes will include a focus on 9-14 year olds and recommendation for vaccinating multiple age cohorts when HPV vaccine is first introduced to result in faster population impact).



**WHO recommends** HPV vaccines should be included in national immunization programmes, provided that: prevention of cervical cancer and/or other HPV-related diseases constitute a public health priority; vaccine introduction is programmatically feasible; sustainable financing can be secured; and the cost effectiveness of vaccination strategies in the country or region is considered.

HPV vaccines should be introduced as part of a coordinated and comprehensive strategy to prevent cervical cancer and other diseases caused by HPV. This strategy should include education about reducing behaviours that increase the risk of acquiring HPV infection, training of health workers and information to women about screening, diagnosis and treatment of precancerous lesions and cancer. The strategy should also include increased access to quality screening and treatment services and to treatment of invasive cancers and palliative care.

The introduction of HPV vaccine should not undermine or divert funding from developing or maintaining effective screening programmes for cervical cancer. HPV vaccination is a primary prevention tool and does not eliminate the need for screening later in life, since the vaccines do not protect against all high risk HPV types.

Opportunities to link the introduction of HPV vaccine to other programmes targeting young people should be sought (e.g. through adolescent health services).

However, the introduction of HPV vaccination should not be deferred because other relevant interventions cannot be implemented at the same time.

Experience with various delivery strategies including campaigns, health facility, and outreach/school-based is still accumulating. Countries should use approaches that are (i) compatible with their delivery infrastructure and cold chain capacity (ii) affordable, cost-effective and sustainable and (iii) achieve the highest possible coverage. If countries consider phased introduction, priority should be given to strategies that include populations which are likely to have less access to screening for cervical cancer later in life.

<sup>8</sup> <http://www.who.int/immunization/documents/positionpapers/en/>

(Continued...)

### Recommended target age and vaccination schedule

- Girls aged 9-14 years\* prior to becoming sexually active.
- 2 doses with a 6 month interval.
- There is no maximum interval between the 2 doses, however, an interval of not greater than 12-15 months is suggested to enable girls to complete the schedule promptly before becoming sexually active.
- If the interval between doses is shorter than 5 months, then a 3rd dose should be given at least 6 months after the first dose.
- A 3-dose schedule (i.e. at 0, 1-2, and 6 months) is recommended for females 15 years and older, and for those known to be immunocompromised and/or HIV-infected (regardless of whether they are receiving antiretroviral therapy). It is not necessary to screen for HPV infection or HIV infection prior to HPV vaccination.

**HPV vaccination of males:** is not recommended as a priority, especially in resource-constrained settings, as the available evidence indicates that the first priority should be for cervical cancer reduction by timely vaccination of young females and high coverage with each dose.

**Vaccine safety:** Both HPV vaccines have excellent safety and efficacy profiles. Adverse events following HPV vaccination are generally non-serious and of short duration.

**Contraindications:** Severe allergic reaction to a previous vaccine dose or vaccine component; Pregnancy; Acute severe febrile illness. However, the presence of a minor infection, such as a cold, is not a contraindication for immunization.

**Co-administration:** HPV vaccine can be co-administered with other non-live and live vaccines using separate syringes and different injection sites.

**Vaccine interchangeability:** The two WHO prequalified HPV vaccines have different characteristics, components and indications, and in settings where both may be in use, every effort should be made to administer the same vaccine for all doses. However, if the vaccine used for prior dose(s) is unknown or unavailable, either of the two HPV vaccines can be used to complete the recommended schedule.

**Monitoring:** As with the introduction of any new vaccine, post-marketing surveillance to monitor safety should be in place. Complete and accurate monitoring of HPV vaccine coverage by dose and by age is needed for programme performance monitoring. Monitoring HPV disease is not a prerequisite to initiating HPV vaccination. However, all countries should consider establishing, or improving, reporting to comprehensive cancer registries or specific cervical cancer registries.

*\*Vaccination of older adolescent females or young women is recommended only if this is feasible, affordable, cost effective, and does not divert resources from vaccinating the primary target population (girls 9-14 years) or from effective cervical cancer screening programmes.*







## 2. DECISION-MAKING AT COUNTRY LEVEL

## WHAT SHOULD BE THE PROCESS?

It is important to have a systematic and transparent process for making a decision about introducing HPV vaccine into the national immunization programme. Ideally, the national immunization technical advisory group (NITAG<sup>1</sup>) or an equivalent independent advisory body should be requested to undertake a rigorous review of the evidence and make an independent recommendation to the national government.

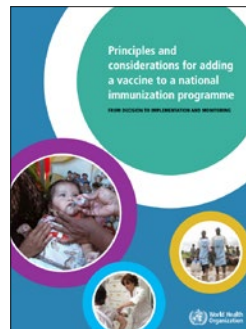
NITAG members should have a broad health perspective to ensure that the impact of HPV vaccine (or any other new vaccine) on the immunization programme and the overall health system is considered.

The NITAG committee and its members must be perceived as objective, independent and not representing a particular interest group. The independence of the NITAG and its reliance on evidence-based decision-making reinforces the credibility of the decision, helps to resist pressure from interest groups and enhances the ability to secure government and/or donor funding for the vaccine introduction. NITAGs function best when they are supported by a secretariat or technical sub-committee to collect and synthesize the evidence.<sup>2</sup>

Subsequently, the Inter-agency Coordinating Committee (ICC)<sup>3</sup> can serve to coordinate partner activities and contribute funding for the immunization programme. As with other decisions pertaining to the national immunization schedule, the national government is responsible for taking the decision to introduce (or not to introduce) HPV vaccine.



### KEY RESOURCE



*Principles and Considerations for adding a vaccine to a national immunization programme: From decision to implementation and monitoring*

A generic guide for countries explaining the principles and issues to be considered when introducing a new vaccine into a national immunization programme.

It describes the process and includes the latest references and tools/checklists for:

- vaccine decision-making
- economic analyses
- developing an introduction plan
- cold chain
- integrated disease control and health promotion
- vaccine safety
- communications
- monitoring

Importantly, this guide highlights ways to use the opportunity of adding a new vaccine to strengthen immunization and health systems.

[http://www.who.int/immunization/programmes\\_systems/policies\\_strategies/vaccine\\_intro\\_resources/nvi\\_guidelines/en/](http://www.who.int/immunization/programmes_systems/policies_strategies/vaccine_intro_resources/nvi_guidelines/en/)

<sup>1</sup> NITAGs should consist of national experts in a broad range of disciplines – such as senior paediatricians, immunization and vaccine experts, epidemiologists, public health experts, health economists, health systems experts and social scientists – who are capable of analysing the different types of scientific evidence and issues that should be considered in making an informed decision.

<sup>2</sup> More information and references on NITAGs can be found at: [http://www.who.int/immunization/sage/national\\_advisory\\_committees/en/](http://www.who.int/immunization/sage/national_advisory_committees/en/)

<sup>3</sup> A committee made up of representatives of the Ministry of Health (MOH), WHO, UNICEF, and other domestic and external partners to improve coordination among partners for the support of the national immunization programme.

Many times a high-level advocate or “champion”, such as the First Lady, can be a key driver to initiate country discussion and decision-making about HPV vaccination. Immunization managers need to be prepared and aware that the first expression of interest about HPV vaccination may come from outside the immunization programme, which enhances the need for the NITAG to be involved.

## WHAT INFORMATION IS NEEDED?

The decision to introduce HPV vaccine needs to consider the following:

- Data on the burden of cervical cancer<sup>4</sup>;
- Existence of a National Cancer (or Cervical Cancer) Strategic Plan;
- Current availability and use of other cervical cancer prevention methods (e.g. screening and treatment);
- Immunization coverage and experiences from any vaccines already given to young adolescents;
- Proposed delivery strategy (or strategies), and an analysis of the proportion of girls who would be reached using the proposed strategy;
- Cost, cost-effectiveness<sup>5</sup>, and affordability;
- Overall capacity and performance of the national immunization programme;
- Experience with HPV vaccine introduction from other countries with similar level of development and health system capacity.

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<sup>4</sup> If local data are incomplete or not available, the International Agency for Research on Cancer (IARC) and WHO **GLOBOCAN** 2012 project (<http://globocan.iarc.fr/>) provides estimates of the incidence of, mortality and prevalence from major types of cancer, at national level, for 184 countries of the world. For a quick access to a summary of the burden of cancer in a country or for a cancer, use the *FACT SHEETS* option. Fact Sheets are a collection of statistical summaries for the eight most common cancer types or for each country or region of the world. They were developed to provide a quick overview of frequently-requested cancer incidence, mortality and prevalence statistics.

<sup>5</sup> The Papillomavirus Rapid Interface for Modelling and Economics (PRIME) model is available to assess cost-effectiveness and health effects of vaccination of girls against HPV before sexual debut in terms of burden of cervical cancer and mortality. See Jit, M. et. al. (2014). Cost-effectiveness of female human papillomavirus vaccination in 179 countries: a PRIME modelling study. *Lancet* Vol. 2, No. 7, e404-e414, July 2014. Available online at: <http://www.thelancet.com/journals/langlo/article/PIIS2214-109X%2814%2970237-2/fulltext?rss=yes>



## RESOURCE EXCERPT

*Scaling-up HPV Vaccine Introduction (WHO, 2016)*

### Decision-making: Implications for Action

- ✓ **Gaining the support of high-level advocates**, such as First Ladies, can have a major impact on the decision to introduce HPV vaccine.
- ✓ **Prepare evidence:** Investigating and reporting on the cervical cancer burden; cost-effectiveness, feasibility and acceptability provides important information for decision-makers.
- ✓ **Coordination with the right stakeholders** from the beginning will ensure all the players are at the table when it's time to make decisions and implement. The Health, Education and Finance Ministries are particularly important.
- ✓ **Prepare for a process involving the policy committees, regulatory bodies, political and financial processes** to ensure the decision is anchored in country policies and budget.
- ✓ **Consider sustainable funding.** Donations and external support can help a country introduce HPV vaccine in the short-term, but countries will need to contribute a portion of funding, and advocates should have a plan to secure funding for longer-term sustainability.

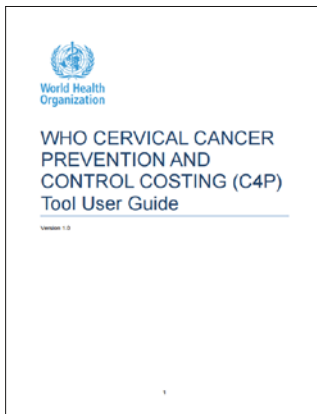
## WILL HPV VACCINATION BE FINANCIALLY SUSTAINABLE?

Financial sustainability is a key cornerstone for any new vaccine introduction. Sustainability for programme administration is more than the ability to purchase HPV vaccine, but also includes financing of any additional expenses incurred by adapting the immunization programme for the introduction or for new delivery strategies. A costing study is a particularly important assessment to conduct for HPV vaccine introduction as the target population has not previously been a part of the routine immunization programme and the delivery of the vaccine may be primarily outside of health centres (at schools or other outreach locations).

WHO has developed a *Cervical Cancer Prevention and Control Costing (C4P) Tool* to assist countries to assess both the financial and economic five-year costs of HPV vaccine introduction (see Key Resource below).



### KEY RESOURCE



### *WHO Cervical Cancer Prevention and Control Costing (C4P) Tool*

Available in both English and French, WHO has developed a generic costing and planning tool for cervical cancer prevention and control. The tool helps programme planners and managers to generate annual cost projections over a five-year period to scale up activities within the health system. The generic version of the WHO C4P tool allows the user to define different vaccine delivery strategies i.e. through schools, health facilities or campaigns, such as national immunization days. Furthermore it allows sub-national segmentation, extensive modification of inputs, a strategic approach, resource allocation, and recognition of prevailing prices and other key variables. It also provides access to transparent underlying calculations and assumptions. The tool is pre-populated with the required data, and linked to data sources.

The WHO C4P tool consists of a HPV Vaccine Module and a Cervical Cancer Screening and Treatment Module.

[http://www.who.int/immunization/diseases/hpv/cervical\\_cancer\\_costing\\_tool/en/](http://www.who.int/immunization/diseases/hpv/cervical_cancer_costing_tool/en/)

### WHAT INFORMATION IS AVAILABLE ABOUT THE PRICE OF HPV VACCINES?

Vaccine product, price, and procurement data are essential to forecasting, budgeting, and identifying sustainable financing for new and priority vaccines. In particular, because vaccine price is an important component of health budgets, the price of a vaccine is a major factor in deciding when to adopt and whether to sustain new vaccines.

However, many countries lack access to information on vaccine prices and can be uncertain about whether they are able to negotiate equitable and fair prices from manufacturers. There have been many calls (particularly from Middle Income Countries) at the World Health Assembly for greater price transparency.

Some vaccine prices are published by individual countries and by large pooled procurement groups such as the UNICEF Supply Division<sup>6</sup> and the PAHO Revolving Fund<sup>7</sup>. WHO has also created a specialize Vaccine Product, Price and Procurement (V3P) Web Platform that brings together price information for all available sources and participating countries (See Key Resource). Information on HPV vaccine prices is included in V3P.

<sup>6</sup> [http://www.unicef.org/supply/index\\_57476.html](http://www.unicef.org/supply/index_57476.html)

<sup>7</sup> [www.paho.org/revolvingfund](http://www.paho.org/revolvingfund)



## KEY RESOURCE

*Vaccine Product, Price and Procurement (V3P) Web Platform*

<http://www.who.int/immunization/v3p>

The V3P web platform provides information on vaccine product, price and procurement data with the goal of increasing price transparency and informing decisions around vaccine introduction and implementation.



The price database contains information on and analyses of vaccine prices and procurement modalities as reported by participating countries and partners, including PAHO revolving fund and UNICEF.



The information repository contains documents produced by V3P, including user guidelines and tools, project updates, and analyses.



The resource gateway is a web portal that offers links to websites providing pertinent information on vaccine product characteristics, price, and procurement.

## WHAT DELIVERY STRATEGY FOR HPV VACCINATION IS BEST?

Deciding the delivery strategy for HPV vaccination is an important issue that needs to be considered carefully by each country. The pros/cons, costs, and likely success of different strategies vary according to the country-specific context.

In general, the ideal strategies for delivery of HPV vaccine should be:

- compatible with existing vaccine-delivery infrastructure and cold chain capacity;
- affordable, cost-effective and sustainable;
- able to achieve the highest possible coverage.

In practice, countries may need to balance strategies that maximize coverage with those considered most feasible, affordable and sustainable.



### Box 2. A word about cost:

Many countries have found that the cost of implementing an HPV vaccination programme is significant. Costs vary by country, by strategy (health facility, school-based or other outreach, campaign), by frequency of vaccination (continuous, monthly, periodic), and by geographical setting (urban, rural, mountainous areas, etc.).

Currently available, preliminary data based on WHO-PATH analysis\* suggest that for GAVI-eligible countries:

- Start-up costs per girl for vaccine delivery are ~ USD\$3-5.
- Operational costs for delivering 2 doses per eligible girl are ~ USD\$3-4.
- During introduction year, total start-up and operational costs for delivering 2 doses per eligible girl is ~ USD\$5-7 (excluding vaccine cost).

*\*Adapted for 2 doses from: Levin A, Wang SA, Levin C, Tsu V, Hutubessy R. Costs of Introducing and Delivering HPV Vaccines in Low and Lower Middle Income Countries: Inputs for GAVI Policy on Introduction Grant Support to Countries. PLoS One, 2014;9(6):e101114.*

In deciding on the delivery strategy for HPV vaccination it is important to prioritize two considerations:

1. Reaching girls who, later in life, will be least likely to have access to cervical cancer screening; and,
2. Wherever possible, selecting approaches that would provide opportunities for integration with other adolescent health services.

It is likely that no single delivery strategy is able to meet all the programme objectives. Ultimately, a combination of strategies may be needed to achieve high coverage and avoid disruption of established services while optimizing resources.

For HPV vaccination there are several commonly used strategies:

- Vaccine delivery at health-care facilities
- Vaccine delivery through outreach:
  - School-based outreach
  - Other outreach
- Vaccine delivery through campaigns

Each strategy has pros and cons. It may be necessary to use a combination of strategies to ensure access for all eligible girls. This is especially true if the young girls targeted for HPV vaccination live both in urban and rural communities, including locations distant from health-care facilities, and if a proportion of them are transient and/or homeless.

### HPV VACCINE DELIVERY AT HEALTH-CARE FACILITIES

Similar to the infant vaccination programme, this approach provides HPV vaccination to eligible girls at a fixed health-care facility. This strategy reduces transport and personnel costs (such as travel allowance) to the health system because it relies on the girls to come to the facility.

Both high and low income countries have shown that it is possible to achieve national HPV vaccine coverage over 70% through offering vaccination at health centres. This strategy has also been

shown to achieve more coverage if offered as “vaccination days” with minor incentives for girls who attend, such as short waiting periods, music, discussion groups and/or videos in the waiting room.

However, a fixed-site, health-care facility delivery strategy may not be effective if girls find it difficult to attend the clinic (for example, if the opening hours are not convenient, or if they are shy or uncomfortable for any reason), or if the majority of girls do not have easy access to a health facility.

School or school health programmes can have an active role in a facility-based delivery strategy. For example, in some countries schools are notified on a specific day to bring girls to the health facility (or nearest scheduled outreach session) for vaccination.

## HPV VACCINE DELIVERY THROUGH OUTREACH

In the context of immunization, outreach refers to any strategy that requires health workers to leave their facility in order to transport and deliver immunization services to a variety of fixed or mobile sites close to large numbers of target-aged girls. Some examples of outreach venues are community centres, school buildings and, if appropriate and with the support of those in charge, places of worship, and other places where people tend to gather.

### School-based (outreach) strategy

For girls living in distant communities and others who cannot attend clinic services, a potential strategy is school-based vaccination. To select eligible girls for vaccination, a school-based strategy may choose to target all girls in one or more selected school year/grade/class, although it is also acceptable to use age-based eligibility.

A school-based strategy can serve as an opportunity to create or strengthen school health services and improve health education and communication.

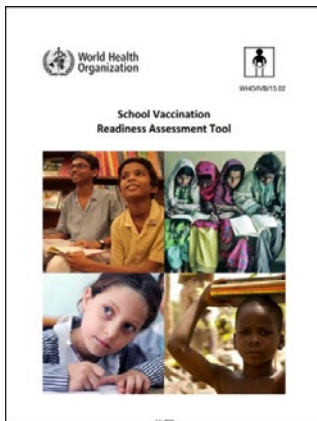
Where school health programmes exist and a designated healthcare worker (based either at the school or health facility), provides regular health services at the school, this person can be trained and charged with vaccinating target-aged girls with HPV vaccine as part of their school-based health duties (if the national policy permits). The operational costs of adding HPV vaccine delivery to an existing and already funded school health programme infrastructure may be minimal (assuming that the costs for salary, per diems, and transport are already provided in the health budget).

If, however, a school health programme with designated healthcare staff does not exist, a school-based delivery strategy will require the health facility staff to travel away from the health centre for several days to reach all the schools in their catchment area. This can be expensive (additional resources needed) and disruptive to regular services to implement. It may also be inefficient if school enrolment of target aged girls is low.

To ensure equitable access to HPV vaccine, where a large proportion of eligible girls are not enrolled in school or there are high rates of absenteeism, a school-based strategy must be supplemented by other efforts to reach girls who are not in school. Teachers and community workers and leaders can play important roles in identifying these girls, educating, motivating and assisting them to access vaccine services at other sites.



## KEY RESOURCE



### *School Vaccination Readiness Assessment Tool*

Before implementing school vaccination programmes, countries need to be able to assess the capacity, strengths, and weaknesses of their school and health systems to support such programmes.

Undertaking a readiness assessment will aid countries in their decision-making and planning, but can also be used by countries wishing to improve the performance of their existing school vaccination activities.

The 3 primary purposes of the School Vaccination Readiness Assessment Tool are:

1. To help Ministries of Health and Education determine, monitor, and improve their country's overall readiness to conduct school vaccination activities.
2. To provide a simple-to-use assessment of a country's overall capacity and specific strengths and weakness to implement school vaccination activities.
3. To guide a process to improve overall readiness and initiation of a new school vaccination programme or to improve an existing one.

While this Readiness Assessment Tool is specifically designed to assess country-wide readiness to implement school vaccination, it might also provide information useful for assessing and subsequently improving broader school health services.

[http://www.who.int/immunization/hpv/plan/school\\_readiness\\_assessment\\_tool\\_who\\_2013.pdf](http://www.who.int/immunization/hpv/plan/school_readiness_assessment_tool_who_2013.pdf)

Education statistics such as those collected by UNESCO<sup>8</sup>, can be useful to gain an understanding of the age profile of those who attend schools and those who do not. Another resource is the “*All in school, Out of school*” reports and online tool<sup>9</sup>.

### Other outreach strategies

When a large proportion of the population lives in areas with limited access to health facilities and there is low school attendance for target-aged girls, an outreach delivery strategy at a convenient location (e.g. marketplace, community gathering place) may be appropriate and help to ensure equitable vaccination opportunities for “hard-to-reach” girls.

Outreach sessions should be planned to ensure all girls are reached with the required HPV doses. The interval between 2 HPV doses must be at least 5 months. Therefore, HPV vaccination outreach sessions could be planned every 6 months, or even annually, to reach all target girls with 2 doses. Depending on the schedule for outreach for infant vaccination, it may be possible to combine it with the HPV vaccination outreach (i.e. offer HPV vaccination at the infant vaccination outreach). This requires good communication and social mobilization so that the girls are informed that vaccination for their age-group is being offered.

As mentioned earlier, some countries are trying an approach where they notify schools on a specific day to bring girls to the nearest scheduled outreach (or fixed facility) for HPV vaccination.

<sup>8</sup> [http://www.uis.unesco.org/\\_LAYOUTS/UNESCO/oosci-data-tool/index-en.html#en/cover](http://www.uis.unesco.org/_LAYOUTS/UNESCO/oosci-data-tool/index-en.html#en/cover)

<sup>9</sup> <http://allinschool.org/resources/reports/>

## VACCINE DELIVERY THROUGH CAMPAIGNS

In some instances, there may be benefits or opportunities to deliver HPV vaccine via a large-scale vaccination campaign strategy.

For example, if a country can afford it and they wish to “catch up” the entire cohort of 9-14 year old girls when the HPV vaccine is first introduced, then planning two rounds of national HPV immunization days with an interval of 6 months, or one campaign annually, may be an option.

Some countries have made use of existing campaign days, e.g. Child Health Days/Weeks, Measles/Rubella or tetanus toxoid (TT) supplementary immunization activities (SIAs), and successfully added HPV vaccination. However, most often the frequency of campaign opportunities that could include HPV vaccination is insufficient to ensure delivery on a routine basis, year after year, of HPV vaccine. Nonetheless, campaigns can be helpful to “kick start” activities.

In countries with very small and difficult to access populations, (for example, island states) the use of a campaign strategy for HPV vaccination may be the most practical and cost-effective. Such countries could conduct a campaign (either with two rounds in a year, or annually for two consecutive years) targeting all the girls 9-14 years. This strategy could be repeated every 5 years to ensure complete coverage of the next cohort of girls 9-14 years.

It is important to note, that any campaign strategy for the delivery of HPV vaccine needs to ensure the recording of the doses administered on the girls vaccination cards. (See Key Resource page 65: *Practical Guide for the design, use and promotion of home-based records in immunization programmes*)

**Table 2** provides summary of considerations for different HPV vaccination delivery strategies. In practice, a balance of the pros and cons will need to be made. Countries may need to consider trade-offs between strategies that maximize coverage and those that are most feasible, affordable, and sustainable. Ultimately, a combination of strategies may be needed to achieve high coverage while optimizing resources. For more information on country experiences using different HPV delivery strategies and reaching hard-to-reach girls see companion document *Scaling-up HPV Introduction* (WHO, 2016).

**Table 2. Considerations for different HPV vaccine delivery strategies**

CONSIDERATIONS	DELIVERY STRATEGY			
	HEALTH FACILITY	SCHOOL-BASED OUTREACH	COMMUNITY OUTREACH	CAMPAIGN
<b>Access</b>	Girls must come to health centre Parents may be present at time of vaccination Does not require health workers to leave post	If enrollment is high, large number of girls vaccinated at the same time Requires health workers to travel to school Parental consent process Teachers can assist with vaccination sessions	A variety of locations possible May need special communications effort to ensure girls come Requires health workers to leave post but can be part of regular health facility outreach	Large number of girls can be vaccinated at the same time Large number of vaccinators needed (may disrupt regular services) Can be used as initial “catch-up” of several age cohorts
<b>Equity</b>	In- and out-of school girls	In-school girls	In- and out-of school girls	In- and out-of school girls

CONSIDERATIONS	DELIVERY STRATEGY			
	HEALTH FACILITY	OUTREACH		CAMPAIGN
		SCHOOL-BASED OUTREACH	COMMUNITY OUTREACH	
<b>Community mobilization</b>	May need more intensive mobilization for girls to attend	Schools can help to facilitate sensitization and mobilization of parents/communities	Same outreach locations as for infant vaccinations may make mobilization easier	Needs strong mobilization effort
<b>Frequency of vaccinations</b>	Continuous vaccine availability possible all year	Requires at least 1-2 visits to schools per year	Vaccine available only when outreach session planned	Requires at least 1-2 rounds per year
<b>Vaccine supply</b>	Continuous vaccine supply available with other routine vaccines	Enrolment lists can facilitate estimates of vaccine supply	Challenging to know exact number of girls who will attend outreach session	Large volume of vaccine needed over short duration Distribution challenges (must be able to redistribute/re-supply quickly during campaign)
<b>Cold chain management</b>	Cold chain available at health centre	Vaccine carriers must be prepared to maintain cold chain	Vaccine carriers must be prepared to maintain cold chain	Vaccine carriers must be prepared to maintain cold chain May be able to use Controlled Temperature Chain (CTC)
<b>Integration with other interventions</b>	Help to strengthen Adolescent Friendly Health Services	Co-delivery with short-duration interventions possible School health platform	Co-delivery with short-duration interventions possible	Integrate with other campaigns (e.g. Child Health Days/Weeks)
<b>Cost</b>	Low as supported by national health budget	Medium-High (depends if school health programme is already funded or if additional resources are required for facility healthcare workers to travel to schools)	Medium-High (depends if using existing outreach sessions that are already planned and funded)	Generally high (but for small populations may be more cost-effective) Additional budget for per-diems and transport, etc.

*Note: A combination of strategies may be needed to achieve high coverage while optimizing resources and to include out-of-school/hard-to-reach/vulnerable target aged girls. Strategies may also vary throughout a country, based on local/provincial/district characteristics or opportunities.*



## HOW CAN HPV VACCINE BE INTEGRATED WITH OTHER VACCINATIONS OR HEALTH INTERVENTIONS?

HPV vaccine introduction may provide impetus to health officials and policy makers to improve and strengthen other health services at national, regional, and local levels. For example, addressing structural or systems barriers that may prevent young adolescent girls from receiving HPV vaccine may facilitate adolescent access to other health interventions. Community health worker networks can be mobilized to assist adolescents in accessing various health services, and vaccine introduction may also serve as an opportunity to improve adolescent health education. Health communication is a key component to successful HPV vaccine implementation, and can be used to deliver a variety of other health messages as well.

**Table 3.** Short duration interventions that may be combined with HPV vaccine delivery

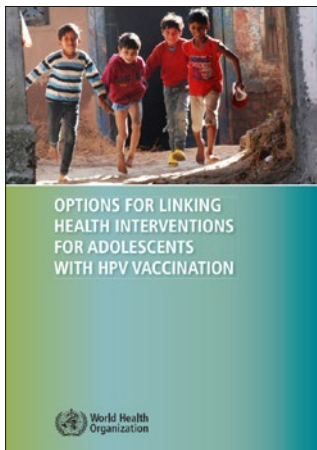
CATEGORY	INTERVENTION
<b>Screening</b>	Vision screening (if referral/glasses available and affordable)
<b>Commodities and treatment</b>	Anti-helminthic treatment (de-worming) Insecticide treated bednets for malaria control Iron and folic acid supplementation
<b>Information and life skills</b>	Promotion of physical activity and exercise Prevention of mosquito-borne diseases Menstrual hygiene education, with products, if relevant for age group targeted for HPV vaccination
<b>Other vaccines</b>	All vaccines can be co-administered with HPV vaccine. Particular opportunities for the target group may be found with Td/Tdap boosters, catch-up of HepB and measles/rubella vaccination, and dengue vaccination (if applicable)

*Adapted from: Hindin M, Bloem P, Ferguson J. Journal of Adolescent Health 2015 Jan;56(1):10-8.*

Delivering HPV vaccination with other interventions may promote sharing of resources and knowledge across programmes, optimize costs and logistics, and serve to integrate a variety of services in a more efficient, effective and sustainable way. It will be important to select an intervention that is age-appropriate, effective, and that will not negatively impact HPV vaccine delivery.



### KEY RESOURCE



#### *Options for linking health interventions for adolescents with HPV vaccination*

There are few interventions targeting young adolescents and those that do exist are often not adequately reaching them. This is because the number of contacts of adolescents with the health system is generally low.

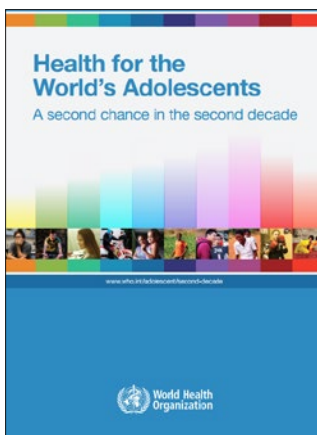
Immunization programmes are well known for achieving good coverage and this short brochure outlines the opportunities that the introduction of HPV vaccination can provide an entry point for other health interventions targeting 9-14 year olds. A number of health interventions are suitable for joint delivery with HPV vaccination and can foster synergies between the Expanded Programme on Immunization (EPI) and school and/or adolescent health programmes.

[www.who.int/immunization/diseases/hpv/linking\\_h\\_interventions/en/](http://www.who.int/immunization/diseases/hpv/linking_h_interventions/en/)

See additional Key Resources on adolescent health below



### KEY RESOURCES – ADOLESCENT HEALTH



*Health for the World's Adolescents* is a dynamic, multi-media, online report. It describes why adolescents need specific attention, distinct from children and adults. It presents a global overview of adolescents' health and health-related behaviours, including the latest data and trends, and discusses the determinants that influence their health and behaviours. It also features adolescents' own perspectives on their health needs.

In addition to the online report, a summary was produced in print format in Arabic, Chinese, English, French, Russian and Spanish.

[http://www.who.int/maternal\\_child\\_adolescent/topics/adolescence/second-decade/en/](http://www.who.int/maternal_child_adolescent/topics/adolescence/second-decade/en/)

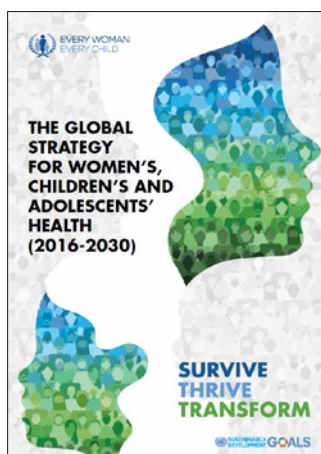


### KEY RESOURCES – ADOLESCENT HEALTH (continued...)

The largest generation of adolescents in human history (1.8 billion) face unprecedented social, economic, and cultural change according to a new *Lancet Report (May 2016): Our Future: A Lancet Commission on Adolescent Health and Wellbeing*.

The Report and related Commission bring together perspectives from public health, economics, political and social science, behavioural science and neuroscience to consider strategies to advance adolescent health and wellbeing, and call for adolescents themselves to be part of the change and accountability mechanisms.

<http://www.thelancet.com/commissions/adolescent-health-and-wellbeing>



To support the implementation of the new Sustainable Development Goals (SDGs) that came into effect January 2016, the UN Secretary-General has called for new and refreshed commitments to the *Every Woman Every Child Global Strategy for Women's, Children's and Adolescents' Health*. For the first time, the health of adolescents has been highlighted for global attention.

[http://globalstrategy.everywomaneverychild.org/pdf/EWEC\\_globalstrategyreport\\_200915\\_FINAL\\_WEB.pdf](http://globalstrategy.everywomaneverychild.org/pdf/EWEC_globalstrategyreport_200915_FINAL_WEB.pdf)

<http://globalstrategy.everywomaneverychild.org/>

As an operational companion guide, the **Global Accelerated Action for the Health of Adolescents (AA-HA!)** will be submitted to the 2017 World Health Assembly. This resource will provide countries with evidence-based interventions and implementation guidance for improving adolescent health.

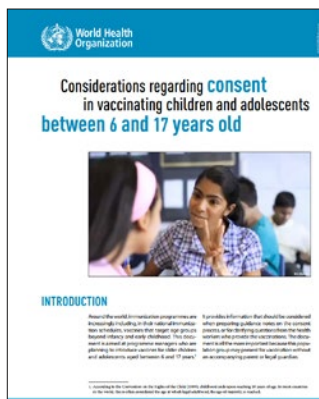
[http://www.who.int/maternal\\_child\\_adolescent/topics/adolescence/framework-consultation-report/en/](http://www.who.int/maternal_child_adolescent/topics/adolescence/framework-consultation-report/en/)

## WHAT POLICIES NEED TO BE IN PLACE?

As a part of the decision-making process for HPV vaccines, the existence and implementation status of the following policy issues should be reviewed:

- Existence of a school health and/or adolescent health programme, services and interventions available, effectiveness and reach of the programme, and links to the national immunization programme.
- Policies and legislation concerning vaccination at school.
- Informed consent process for routine immunization services and vaccines delivered during campaigns, and the applicability of these policies for HPV vaccines delivered to girls aged 9–14 years.
- Policies and strategic plans related to the prevention of cervical cancer, and the potential role of HPV vaccination in these policies and plans.

### KEY RESOURCE



### *Considerations regarding consent in vaccinating children and adolescents between 6 and 17 years old*

Around the world, immunization programmes are increasingly including, in their national immunization schedules, vaccines that target age groups beyond infancy and early childhood.

This document is aimed at programme managers who are planning to introduce vaccines for older children and adolescents aged between 6 and 17 years.

It provides information that should be considered when preparing guidance notes on the consent process, or for clarifying questions from the health workers who provide the vaccinations.

The document is all the more important because the target population group for HPV vaccine may present for vaccination without an accompanying parent or legal guardian.

[www.who.int/immunization/programmes\\_systems/policies\\_strategies/consent\\_note/en/](http://www.who.int/immunization/programmes_systems/policies_strategies/consent_note/en/)

## WHO ARE KEY STAKEHOLDERS TO INCLUDE IN THE PROCESS?

Successful introduction of HPV vaccine as part of a comprehensive cervical cancer control strategy will require collaboration of the immunization programme with a variety of stakeholders within and across programmes and sectors at different levels of government.

Close collaborations with cancer, adolescent health, women's health, and/or sexual and reproductive health programmes can foster supportive partnerships for HPV vaccine introduction. School-based strategies are an opportunity to collaborate with school health programmes where they exist, and more broadly, with the Ministry of Education to integrate public health messages within schools. Ongoing communication among stakeholders before, during, and after vaccine introduction is essential for successful implementation.

Advocacy with and engagement of medical and nursing associations, national leaders, parliamentarians, and other stakeholders will be essential to ensure high HPV vaccination coverage and awareness of the need to strengthen cervical cancer screening.

Ultimately, a country should have developed a National Cancer Strategy within which activities to prevent cervical cancer are situated. It is similarly important for countries to establish population-based cancer registries<sup>10</sup> in order to measure the burden of cancer in communities and assess the impact of interventions.

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<sup>10</sup> IARC Technical Publication No. 43. 2014. Planning and developing population-based cancer registration in low and middle income settings. <http://www.iarc.fr/en/publications/pdfs-online/treport-pub/treport-pub43/>



### 3. PLANNING

## WHAT PLANS NEED TO BE MADE OR REVISED?

Once a decision has been taken to introduce HPV vaccine, a detailed planning process will need to be conducted. The target population, delivery strategy, vaccination schedule, and logistics need to be carefully considered and the national comprehensive multi-year plan for immunization (cMYP) updated. Step-by-step guidance is provided in the *WHO/UNICEF Guidelines for developing a comprehensive multi-year plan (cMYP)* document available from the WHO website<sup>1</sup>.

In addition to updating the cMYP to include HPV vaccine, a detailed introduction plan will need to be developed. The plan should outline all activities and steps required for a successful introduction by programme component, identify government departments, institutions or external partners that are responsible for each activity, and include a timeline and detailed budget.

Given the unique considerations for HPV vaccine introduction, it is critical that countries allow enough time for planning and implementation of all the specified introduction activities and that the introduction is not rushed. Sequencing activities in a detailed chronogram will highlight critical milestones necessary for the HPV vaccine introduction to proceed smoothly.

Countries are encouraged to refer to the checklist and tools contained in the WHO guide *Principles and considerations for adding a new vaccine to a national immunization programme: From decision to implementation and monitoring* (See Key Resource page 13). In particular:

Annex 3: Template for a new vaccine introduction plan.

Annex 4: New vaccine introduction checklist, activity list, & timeline.

Both of these annexes can be downloaded in an Excel format.<sup>2</sup>

## HOW TO PLAN FOR NATIONAL INTRODUCTION?

Immunization programmes without prior experience of routinely delivering multi-dose vaccinations to 9-14 year old girls may benefit by planning a phased introduction of HPV vaccine. This enables the identification and resolution of challenges and barriers before national scale-up.

Delivering HPV vaccine on a small scale (e.g. 1-2 districts or states/provinces with different characteristics such as, urban/rural, high/low coverage, different levels of school attendance, etc.) allows the national immunization programme to:

- fine tune training and communication plans
- evaluate vaccine acceptability by the community and health professionals
- determine the communication and social mobilization strategies necessary to establish and sustain high coverage for HPV vaccine
- learn how to best access the target age group
- identify the human and financial resources required
- consider whether the proposed delivery strategies are sustainable

<sup>1</sup> [http://www.who.int/immunization/programmes\\_systems/financing/tools/cmyp/en/](http://www.who.int/immunization/programmes_systems/financing/tools/cmyp/en/)

<sup>2</sup> [http://www.who.int/immunization/programmes\\_systems/policies\\_strategies/vaccine\\_intro\\_resources/nvi\\_guidelines/en/](http://www.who.int/immunization/programmes_systems/policies_strategies/vaccine_intro_resources/nvi_guidelines/en/)

## HOW TO SELECT THE TARGET POPULATION FOR HPV VACCINATION?

National strategies for HPV vaccination should prioritize high coverage in the primary target population of 9-14 year old girls, prior to the onset of sexual activity, as HPV vaccination is most effective when administered prior to exposure to HPV types in the vaccine.

WHO now recommends the vaccination of multiple cohorts of girls 9-14 years when HPV vaccine is first introduced. This has cost implications but results in faster population impact than vaccination of single age cohorts. After the initial vaccination of all girls 9-14 years (or some subset), in the subsequent years going forward, only one age cohort will need to be targeted (e.g. 9 year old girls).

However, if countries have resource limitations that prevent initial multiple cohort vaccination, a single year cohort (or school grade) of girls within the age range of 9-14 years can be selected as the target population for HPV vaccination.

Deciding which age or grade cohort to target for HPV vaccination is an important decision that should consider local factors such as:

- Average age of becoming sexually active. For example, if it is common for girls to marry at 12-14 years of age, then it would be best to provide HPV vaccine at a younger age.
- If knowledge of age is culturally or socially unimportant/limited, it may be better to target an age that is a rounded number for example, 10 years, rather than 9 or 11 years. Anecdotally, it is reported that recall of whole years is more accurate.
- If girls tend to drop-out of school as they get older, it may be better to target the earlier school grades.
- Etc... Consider whatever information is relevant for the particular country context.

Ideally, the choice of what age cohort or grade to target for HPV vaccination should be driven by a good understanding of where the highest number of girls can be found and easily reached, in order to achieve high coverage.

### HOW TO DETERMINE THE AGE OF GIRLS WHO ARE ELIGIBLE FOR HPV VACCINATION?

Once a specific target age group has been chosen, the next step is to decide how this age will be determined in order to identify the girls who are eligible for HPV vaccination. There are two common practices:

- By age at time of vaccination, e.g. all 10 year old girls;
- By year of birth, e.g. all girls born in the year 2005.

Deciding which approach to use will depend upon the delivery strategy and the frequency of vaccination contacts (e.g. continuous if facility-based, or 1-2 times per year if outreach) and the level of knowledge/documentation of birth dates.

#### **By age at time of vaccination, e.g. all 10 year old girls**

With this approach, eligibility for HPV vaccination is based on the age at the time of the first dose, using the date of birth of the girl – at least the month and the year.

Regardless of the location of vaccination (at the health facility or at an outreach site, such as a school) this approach requires the girls to know their age, or for the vaccinator to have access to some documentation (e.g. register, enrolment list) for which the age of the girl can be confirmed.



Determining eligibility using “age at time of vaccination” is an approach which is best suited to strategies that offer HPV vaccination continuously – for example, facility-based vaccination. Girls are told to come for vaccination when they have reached a certain age, if they come before then they are told to return after they have had their birthday. There is a risk that they will forget or not be able to return, but if they do, the HPV vaccine will be administered to them.

Determining eligibility by “age at time of vaccination” can be problematic for outreach strategies that take place only once or twice a year. For example, for a twice yearly school-based outreach, not all girls will have had their birthday when the outreach vaccination team visits. Some may only be of eligible age at the time of the 2<sup>nd</sup> outreach visit (so they can get their first dose then) but they will have to wait until the next time to complete their schedule.

### By year of birth e.g. all girls born in the year 2005

Eligibility for vaccination based on the “year of birth” may be programmatically easier to implement for all delivery strategies. This approach determines, for example, that all girls born in 2005 are eligible because they all will have turned 10 years of age by the end of calendar year 2015. In this scenario, when the HPV vaccine is introduced it is announced that all girls born in 2005 should receive HPV vaccination. Regardless of when the vaccine doses are offered or administered, the cohort who is eligible in that year receives the vaccination. Additionally, in places with limited knowledge or records for exact date of birth, girls, parents, health workers, and teachers may be more likely to know or determine a year of birth using significant events or cultural milestones as reminders.



### **Box 3. A word on using a single school grade/class as a “proxy” for the target for HPV vaccination (e.g. all girls enrolled in primary school Grade/Class 5)**

For countries that are planning to deliver HPV vaccination primarily using a school-based outreach strategy it may be tempting to simply select the girls in a particular grade as the target population (e.g. all the girls in Grade/Class 5). However, caution is advised. A grade/class is a proxy for girl’s year of age, not the other way around. If a grade-based target group is to be used, it must be chosen following an assessment of the age span in the grade.

For example, if a country decides to vaccinate 10 year old girls then it is necessary to find out what percent of girls are 10 years old in each grade. If analysis reveals that only 50% of the girls in Grade 5 are 10 years old, and that the others range in age from 8-14 years then obviously vaccinating all the girls in Grade 5 will not achieve the programmes target and it will be very difficult to calculate any meaningful coverage rate.

However, if for an example in another country, following an assessment it is confirmed that majority of the 10 year old girls are to be found in Grade 5 – then indeed it may be operationally appropriate to select all the girls in Grade 5 for vaccination and not worry that a few who are older/younger will be vaccinated also. Overall, in this example, the target population is those girls who are 10 years old. Such an approach would need to assure that school enrolment levels were sufficiently high that there were not a lot of 10 year old “out of school” girls who would be missed. Even if the numbers are small, complementary strategies to reach and vaccinate out of school girls are required.



**Box 3. A word on using a single school grade/class as a “proxy” for the target for HPV vaccination (e.g. all girls enrolled in primary school Grade/Class 5) (continued...)**

With a grade based approach one needs to be careful that girls in the selected grade who are too young to be vaccinated are not missed the subsequent year when they will be of eligible age for vaccination but will now have moved on to a grade higher.

As illustrated in the examples above, grade-based targeting can be very tricky and requires a good deal of formative research to carefully understand the age composition of various grades. Moreover, it is likely that the age-distribution of a grade in one part of the country will differ from others (e.g. urban vs rural schools) and in fact, may change overtime as more and more girls are encouraged to attend, and remain in, school.

## HOW CAN THE NUMBER OF GIRLS TO BE VACCINATED WITH HPV VACCINE BE ESTIMATED?

In order to plan, forecast vaccine supply, and be able to calculate coverage, an accurate estimate of the number of girls in the target age group is required. Ideally, countries should make this calculation using up-to-date national or local census data obtained from national statistical offices.

If such census data are not available, are inaccurate or are out-of-date (as is often the case), it is possible to obtain single age annual population estimates for females (and also males) by country from the United Nations Population Division website.<sup>3</sup> These data are revised every two years.

See **Annex 1** for an example of how to access this UNPop data file for females.

WHO will be using these UN Population Division estimates by single year of age to calculate future WHO-UNICEF estimates of national immunization coverage (WUENIC) for HPV vaccine by country and globally.

To make access and use of the UN Population Division data easier for countries and partners, WHO has extracted the population estimates for every country by year, sex and single year of age for the years 2010-2020 specifically for the 9-13<sup>4</sup> year old population. These data may be used freely and are available from the WHO website<sup>5</sup>. They will be updated every two years when UNPop Division publishes its revision.

The data are in an Excel interactive pivot table database which may be accessed in English, French or Spanish and allows users to select the country and specific single-year-of-age target population(s) that have been chosen for HPV vaccination. Population estimates for boys are also provided to facilitate planning for the delivery of adjunct health interventions to all adolescents (males and females) as part of integrated approaches to adolescent and school health service delivery.

<sup>3</sup> <http://esa.un.org/unpd/wpp/Excel-Data/population.htm>

<sup>4</sup> The next revision will extract population estimates for the 9-14 year old population, in line with the updated recommended target age range.

<sup>5</sup> The suggested citation is: World Health Organization, Department of Immunization, Vaccines and Biologicals. Projections of national annual population 9-14 years of age by single year of age and sex, 2010-2020. Geneva; 2012. [http://www.who.int/immunization/diseases/hpv/UN\\_population\\_estimates\\_9-14\\_year-old\\_cohort/en/](http://www.who.int/immunization/diseases/hpv/UN_population_estimates_9-14_year-old_cohort/en/)

## WHERE CAN YOU FIND THE GIRLS TARGETED FOR HPV VACCINATION?


Once the target population and its size has been determined, it is necessary to understand where the girls may be located in order to plan an appropriate delivery strategy. Girls who are attending school may be found at schools; however, not all girls attend school. Out of school girls may be dispersed and difficult to locate. They may be in the formal or informal labour market, assisting families with agriculture, household chores, tending livestock, or other activities in the community. Reaching girls who are members of pastoralist communities or live in remote locations may require specific strategies.

Countries are encouraged to work with education, census, labour, school health and other sectors to map the situation in their country, including estimations of the proportion of girls attending / not attending schools in all districts. Consultation with district leaders in a variety of geographic settings may also yield useful information about the local situation where girls of the target age range of 9-14 years old may be found. Recent experiences by the EPI programme in organizing vaccination campaigns targeting older children, such as Meningitis A or measles, may provide additional insight into ways to access young adolescent girls.

## HOW MUCH WILL IT COST TO INTRODUCE HPV VACCINE?

Adding HPV vaccine to the national immunization programme will have cost implications (see previous section on financial sustainability and Box 2 on Costs page 18).

The immunization programme budget and financing plan will need to be updated. WHO has developed and field-tested a *Cervical Cancer Prevention and Control Costing (C4P) Tool* (see Key Resource page 17) to assist countries in determining actual costs and making five-year projections of both financial and economic costs for HPV vaccine introduction.



For more information on country experiences regarding HPV vaccine costing, financing and sustainability see companion document *Scaling-up HPV Vaccine Introduction* (WHO, 2016).

**Box 4: Possible costs to include when budgeting for HPV vaccine introduction**

- Procurement of vaccine, injection materials, and safety boxes.
- Training of all relevant health workers at all levels.
- Orientation to school staff, if vaccinations will occur at schools.
- Increased frequency of health workers leaving post for delivery through outreach.
- Expansion of the cold chain, dry storage, vaccine transport systems.
- Extra fuel expenses for cold chain and transport.
- Possible additional health personnel costs for outreach, mobile units, school delivery.
- Repairs, expansion or addition of waste management facilities to handle the additional waste generated.
- Development of materials for community sensitization and mobilization.
- Implementing comprehensive community sensitization and mobilization activities.
- Advocacy activities with key stakeholders at national, subnational, and district levels.
- Revision and printing of standard immunization forms, such as vaccination cards, tally sheets, registers, monitoring forms, guidelines, etc.
- Strengthening AEFI surveillance, reporting, and management.

## HOW TO COORDINATE WITH OTHER STAKEHOLDERS?

Because HPV vaccine introduction should be a part of a comprehensive and integrated health strategy to prevent cervical cancer, it is important that the efforts of the EPI programme are closely coordinated with other stakeholders. Involvement of women's health, cancer control, school health, adolescent health, sexual and reproductive health, non-communicable disease control, Ministry of Education, and other groups has advantages in building a strong advocacy network for achievement of a shared goal. However, collaborating with cancer control or women's health or the Ministry of Education may be new for many national immunization programmes.

Other stakeholders who may influence the environment of support for HPV vaccine introduction may include medical and nursing associations, women's rights and gender equity advocates, civil society organizations, government officials, parliamentarians, and even the media. Countries need to carefully consider which stakeholders are critical and supportive of HPV vaccines as a viable mechanism for cervical cancer prevention. It is also necessary to distinguish between those stakeholders/partners to be engaged in decision-making and planning, from those needed for advocacy and community engagement.

HPV vaccination targets adolescent girls. Therefore it can use platforms that may exist in countries for the delivery of other interventions for adolescent health, such as for example deworming, micronutrient supplementation, health promotion or health screening activities. These activities may be implemented through comprehensive school health or adolescent health programmes, or by programmes that focus on specific diseases such as neglected tropical diseases in the case of deworming.

HPV vaccination may provide an opportunity to deliver or expand the coverage of other adolescent health interventions. Conversely, existing programmes such as the regular distribution of deworming pills or Iron Folic Acid supplements may be opportunities to efficiently co-deliver the HPV vaccine<sup>6</sup>.

Generally, convening an oversight committee (such as the Inter-Agency Coordinating Committee – ICC) has proven to be an effective mechanism to coordinate and collaborate with the diverse set of stakeholders who need to be engaged for successful HPV vaccine introductions. Many countries created a national level planning committee led by the Ministry of Health/EPI in close coordination with the Ministry of Education (for school-based delivery). Creating a series of sub-committees for activities such as Communications, Training, Vaccine Management and Logistics, and Monitoring and Evaluation, and holding regular meetings of these committees (e.g. weekly) helps to keep work-plans on track.

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<sup>6</sup> See Key Resource page 20 "Options for linking health interventions for adolescents with HPV vaccination. [www.who.int/immunization/diseases/hpv/linking\\_h\\_interventions/en/](http://www.who.int/immunization/diseases/hpv/linking_h_interventions/en/)



## 4. VACCINE MANAGEMENT

# HOW TO FORECAST AND CALCULATE VACCINE SUPPLY NEEDED FOR HPV VACCINE?

In general, HPV vaccine introduction should follow the standard procedures for calculating vaccine supply of other vaccines and be integrated into existing mechanisms to order other vaccines. HPV vaccine should also be integrated into the stock-management system and vaccine orders must be timed such that the supply is not disrupted.

Doses required for the annual supply is based on the size of the target population, estimates of vaccine coverage of the first dose, and vaccine wastage. The simple formula below can assist:



\* Estimated vaccine coverage for dose 1 assumes no drop-out between dose 1 and dose 2.

† Wastage factor must be adjusted for 1-dose or 2-dose vials.

# WHAT COLD CHAIN CAPACITY WILL BE REQUIRED FOR HPV VACCINE?

The presentations available for each HPV vaccine are listed in the table below.

Table 4. Summary of HPV vaccine packaging and presentations

ATTRIBUTES	BIVALENT (CERVARIX®)	QUADRIVALENT (GARDASIL®/SILGARD®)	9-VALENT (GARDASIL 9®)
Vaccine picture			
Presentation	Liquid, 1-dose and 2 dose vials	Liquid, 1 dose vial	Liquid, 1 dose vial
Preservative	No preservative for either presentation	No preservative	No preservative

ATTRIBUTES	BIVALENT (CERVARIX®)		QUADRIVALENT (GARDASIL®/SILGARD®)	9-VALENT (GARDASIL 9®)
<b>Packaging for cold chain volume</b>	1 dose vial, box of 1: 57.7 cm <sup>3</sup> /dose	2 dose vial, box of 1: 28.8 cm <sup>3</sup> /dose	1 dose vial, box of 1: 75.0 cm <sup>3</sup> /dose	1 dose vial, box of 10: 15.0 cm <sup>3</sup> /dose
	1 dose vial, box of 10: 11.5 cm <sup>3</sup> /dose	2 dose vial, box of 10: 5.7 cm <sup>3</sup> /dose	1 dose vial, box of 10: 15.0 cm <sup>3</sup> /dose	
	1 dose vial, box of 100: 9.7 cm <sup>3</sup> /dose	2 dose vial, box of 100: 4.8 cm <sup>3</sup> /dose		
<b>Storage requirements</b>	<ul style="list-style-type: none"> <li>Kept at 2°-8° C</li> <li>Should not be frozen</li> <li>Protected from light</li> </ul>		<ul style="list-style-type: none"> <li>Kept at 2°-8° C</li> <li>Should not be frozen</li> <li>Protected from light</li> <li>Licensed for use in CTC (up to 3 days, up to 42<sup>0</sup>)</li> </ul>	<ul style="list-style-type: none"> <li>Kept at 2°-8° C</li> <li>Should not be frozen</li> <li>Protected from light</li> </ul>
<b>Shelf life</b>	1 dose vials: 48 months at 2°-8° C	2 dose vials: 36 months at 2°-8° C	36 months at 2°-8° C	36 months at 2°-8° C
<b>VVM</b>	Type 30		Type 30	TBD
<b>Wastage rate</b>	1-dose vials	2-dose vials	1-dose vials	1-dose vials
<b>Wastage factors</b>	<5%	10%	<5%	<5%
	1.05	1.10	1.05	1.05

Additional information on the different HPV vaccines is available on the WHO website at [http://www.who.int/immunization\\_standards/vaccine\\_quality/PQ\\_vaccine\\_list\\_en/en/index.html](http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/index.html).

Adequate refrigerator space must be available for storage of vaccines at +2 to +8°C. The WHO Vaccine Volume Calculator<sup>1</sup> tool is available to help assist in calculation of cold chain capacity requirements for the amount of vaccine needed. Adequate dry storage will also need to be available for the additional injection materials, such as syringes, and safety boxes that will be needed for delivery of HPV vaccines.

## HOW SHOULD HPV VACCINES BE STORED AND HANDLED?

### HPV VACCINE STORAGE

HPV vaccine management should follow the same procedures as for other vaccines in the cold chain. Upon receipt and confirmation of quantity delivered, the vaccines should be placed in designated refrigerators. All HPV vaccines should be stored between +2° to +8°C.



Regular temperature monitoring procedures should be maintained in all cold storage equipment and **checked twice daily** every day of the year, including weekends and holidays.

<sup>1</sup> [http://www.who.int/immunization/programmes\\_systems/supply\\_chain/resources/tools/en/index4.html](http://www.who.int/immunization/programmes_systems/supply_chain/resources/tools/en/index4.html)



HPV vaccines SHOULD NOT BE FROZEN as they are exceptionally sensitive to temperatures lower than +2° C and lose efficacy if frozen. Vaccines subjected to temperatures lower than +2° C should not be used. If there is suspicion that a vaccine has been frozen, a shake test should be performed. **Annex 2** provides the WHO protocol for a shake test.

HPV vaccines cannot be placed directly on or near the freezer portion of refrigerators, and HPV vaccines should not be stored near the liners or walls of cold boxes and or ice-packs in vaccine carriers. Proper procedures for conditioning ice-packs in vaccine carriers or use of cold packs in vaccine carriers should be followed. WHO guidance on these procedures is available in the following documents: *Immunization In Practice: A Practical Guide for Health Staff, Module 2 – The Vaccine Cold Chain*<sup>2</sup> and the *WHO Vaccine Management Handbook* modules<sup>3</sup>.

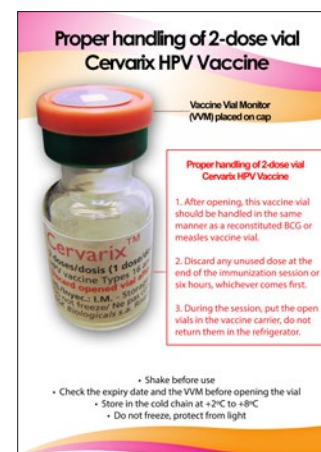
HPV vaccines are sensitive to light and should be stored in the original box until ready to use.

Under special conditions, some HPV vaccine products are licenced for Controlled Temperature Chain (CTC) which permits the vaccine to be kept at ambient temperatures not exceeding 42° C for up to 72 hours (See **Box 1** page 6 for details).

## HPV VACCINE HANDLING

For use of 2-dose vials of **bivalent** HPV vaccine, countries should ensure that health workers are trained on appropriate handling of unpreserved multi-dose vials, per the guidelines set out in the WHO multi-dose vial policy<sup>4</sup> (see Box 5).

Opened vials of the product should be discarded at the end of the immunization session or after 6 hours, whichever comes first. Each vial contains a vaccine vial monitor (VVM) to indicate cumulative exposure to heat. The VVM provides a warning when the vaccine is likely to have been degraded and should be discarded. Both HPV vaccines have been certified for VVM type 30. It is important to highlight that the VVM does NOT alert about vaccine freezing.



<sup>2</sup> [http://www.who.int/immunization/documents/IIP2015\\_Module2.pdf](http://www.who.int/immunization/documents/IIP2015_Module2.pdf)

<sup>3</sup> [http://www.who.int/immunization/programmes\\_systems/supply\\_chain/evm/en/index5.html](http://www.who.int/immunization/programmes_systems/supply_chain/evm/en/index5.html)

<sup>4</sup> WHO Statement on Multi-dose Vial Policy (MDVP), Revision 2014. [http://www.who.int/immunization/documents/general/WHO\\_IVB\\_14.07/en/](http://www.who.int/immunization/documents/general/WHO_IVB_14.07/en/)



### Box 5: WHO requirements for 2-dose presentation of preservative-free Cervarix™\*

Special attention to training of health care staff will be required for the proper use of the Cervarix™ two-dose presentation because it is a multi-dose preservative-free vaccine. Specific pre-introduction measures are required to assure programmatic readiness is achieved prior to introduction.

To mitigate against potential programmatic risk countries should ensure that they:

- Understand the benefits and potential contamination risks of the two-dose unpreserved presentation and understand the need for special training and good supervision to enhance immunization worker practices.
- Conduct post introduction evaluations to determine levels of Health Care Worker knowledge and compliance with the correct handling of the vaccine; and implement corrective training if needed.

Prior to introduction and before UNICEF Supply Division will ship the vaccine countries must:

- Ensure training materials are in place in immunization centres prior to the launch of the vaccine.
- Place stickers on refrigerators at all levels indicating that opened vials of the vaccine must be discarded six hours after opening. The stickers should be in place prior to the launch of the vaccine.

\*[http://www.who.int/immunization\\_standards/vaccine\\_quality/cervarix\\_pqnote\\_2dose\\_2013/en/index.htm](http://www.who.int/immunization_standards/vaccine_quality/cervarix_pqnote_2dose_2013/en/index.htm)



### Box 6: NEW VVM Infographic

WHO has just released a new infographic that summarises how health workers can use vaccine vial monitors (VVMs) to decide whether or not to use a vaccine vial. Most notably, it presents VVM colour change as a continuous progression, rather than as four distinct stages.

A VVM is a chemical indicator label attached to the vaccine container (vial, ampoule or dropper) by the vaccine manufacturer. As the container moves through the supply chain, the VVM records its cumulative heat exposure through a gradual change in colour. If the colour of the inner square is the same colour or darker than the outer circle, the vaccine has been exposed to too much heat and should be discarded.

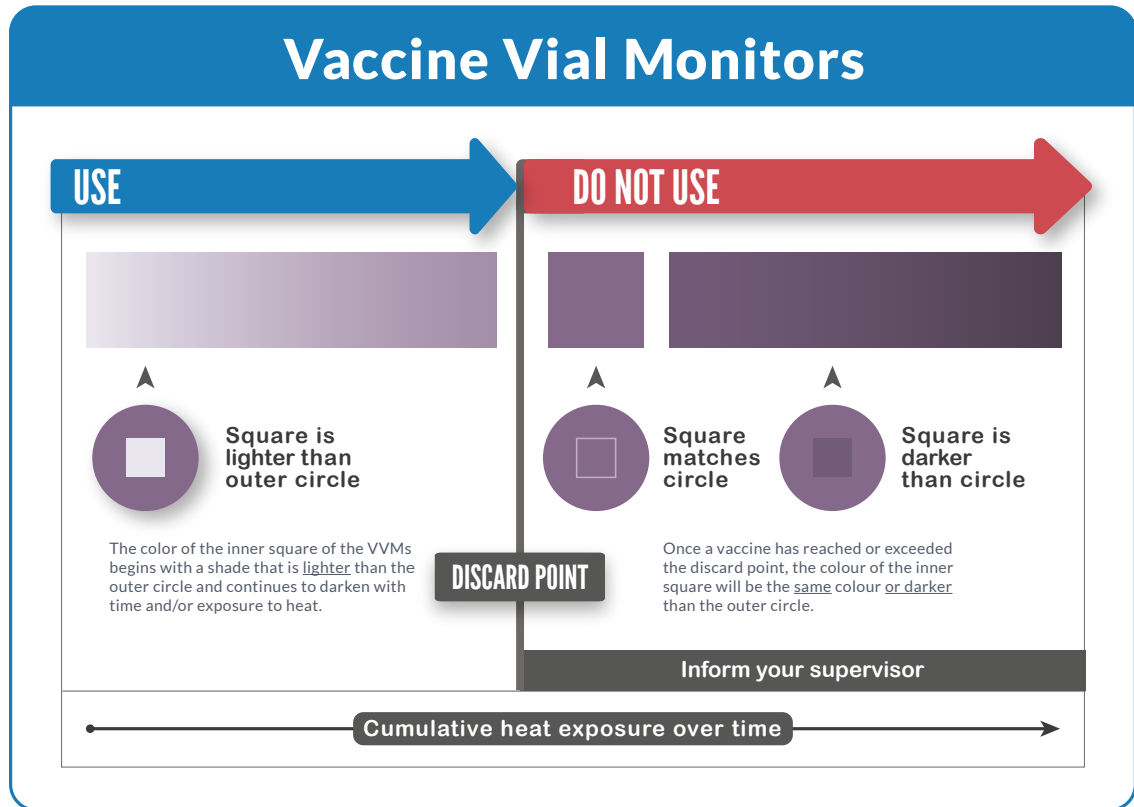
The main purpose of VVMs is to ensure that heat-damaged vaccines are not administered. The VVM status is also used to decide which vaccines can safely be kept after a cold chain break occurs thus minimizing unnecessary vaccine wastage. In addition, VVM status helps the user decide which vaccine should be used first – a batch of vaccine showing significant heat exposure should be distributed and used before a batch that shows lower heat exposure, even if its expiry date is longer.



### Box 6: NEW VVM Infographic (continued...)

Please use the new infographic in guidance and training materials, and share widely. The infographic is available in English and French on the WHO website:

[http://www.who.int/immunization/programmes\\_systems/supply\\_chain/resources/tools/en/index4.html](http://www.who.int/immunization/programmes_systems/supply_chain/resources/tools/en/index4.html)



## WHAT IMPACT WILL HPV VACCINE INTRODUCTION HAVE ON WASTE MANAGEMENT?

As with any new vaccine introduction, HPV vaccine introduction will generate additional vaccine waste that requires appropriate disposal. All current waste management facilities should be reviewed to ensure there is adequate capacity to handle increased waste volume generated by HPV vaccine delivery.

The impact on the waste management system will depend on the delivery strategy. It is likely to be greater if HPV vaccine is delivered in a campaign-style twice a year, than for continuous delivery of HPV vaccine at health centres throughout the year, which will increase the waste volume but in a more stable manner. Countries should carefully plan for the frequency and amount of increased waste.



## 5. MICROPLANNING AT THE DISTRICT LEVEL

Adequate microplanning at the district level prior to introduction is essential. In particular, for HPV vaccine delivery there are a few issues that need careful consideration.

## VERIFYING THE ESTIMATED TARGET POPULATION

Estimates of the target population will have most likely been made using national or subnational data extrapolated from the last census. Because population movements can be significant and local circumstances may have changed, it is important to verify estimates of the eligible population at the district level for each district in the country. This is sometimes referred to as enumeration.

District health and education leaders should be involved, especially if schools will be a part of the vaccine delivery strategy. Checking for new schools that have opened or schools that have closed may also have an impact on the overall estimates of the eligible population in the district.

For enumeration for school-based strategies, the following steps are suggested:

- Generate an up-to-date list of all schools in the district (including private schools and special education schools which may be missing from official lists).
- Contact the schools and obtain the number of target girls who are enrolled.
- If possible, have the school pre-register or enumerate the girls who are to be vaccinated and provide a list of the girl's names and dates of birth to the health facility.
- Confirm with the schools and obtain agreement that the dates proposed for vaccination are convenient and do not conflict with school exams or holiday periods.

For enumeration for community outreach strategies:

- Involve volunteer health workers and community members to generate up-to-date lists of girls of eligible age who do not attend school.

Naturally occurring events, such as agriculture migration or natural disasters, could also influence population estimates. Seasonality could also be a factor if populations move when vaccinations are scheduled in local areas. Planning for these known seasonal migration patterns can help ensure more accurate projections of the number of eligible girls who may be available for vaccination. Conflict, famine, and political stability may also be localized events impacting the movement of people. Understanding if this situation is present can help inform the estimates of the target population as well.

## ENSURING THAT COLD CHAIN CAPACITY IS ADEQUATE

Management of HPV vaccine in local health centres should follow the same procedures as is done for any vaccine requiring continuous cold chain. A quality and recent effective vaccine management (EVM) assessment can inform if any health facilities require cold chain expansion, maintenance or strengthening in advance of HPV vaccine introduction. Similarly, it will be necessary to ensure that the health facility has sufficient vaccine carriers and cold-packs if HPV vaccination will be conducted via outreach to schools and communities. Transportation costs and per diems also need to be included.

Vaccine logistics will be impacted by the chosen delivery approach. Offering HPV vaccine throughout the year alongside routine infant vaccinations will have different implications for the logistics, forecasting and supply than providing HPV vaccine only periodically (e.g. once or twice a year). The microplanning process needs to consider this when preparing health facilities for HPV vaccine introduction.

# PLANNING AND COORDINATING LOGISTICS FOR VACCINE DELIVERY AT OUTREACH LOCATIONS IN SCHOOLS AND COMMUNITIES

Logistics for vaccinations at outreach locations or at schools requires careful planning and advanced coordination to ensure efficient implementation, as health workers will be leaving the health post. See **Box 7** below for a microplanning checklist for HPV vaccination outreach sessions.



## **Box 7. Microplanning checklist for HPV vaccine delivery at schools and outreach locations**

- Vaccine delivery outside of health centres may result in additional costs. These costs should be planned for and secured prior to delivery.
- Ensure that the human resources needed to carry out the outreach are arranged without disrupting services at the health centre.
- Map all health centres and health posts in the district and all schools and outreach locations to be reached.
- Coordinate with district education officials to ensure all schools are accounted for in the mapping exercise.
- Try to arrange HPV vaccination at schools and outreach locations to be conducted by the nearest health facility/post in that catchment area. This helps to reduce transportation costs, shortens the distance to carry vaccines and supplies, and supports building positive relations between the local staff at health centres with the surrounding community.
- Assess opportunities to combine HPV vaccination outreach with other outreach activities for integrated delivery with other health interventions.
- Coordinate closely with school administration, headmasters, and education officials to set dates for vaccination that do not conflict with school exams and holidays and which reduce disruption to regular classes.
- Pay particular attention to private schools, religious and other schools that are not part of the public school network.
- Make sure that parents/communities are informed in advance that HPV vaccination will take place, and that consent is given (see section below for consent options).
- If an entire group of girls is to be vaccinated at once, the time needed for one health worker to vaccinate twenty girls is approximately one hour.
- Districts should consider utilizing more health workers at larger schools or outreach sessions to ensure all girls mobilized for vaccination can be accommodated in a single session.
- Repeated visits to schools or outreach locations for girls missed should be balanced against time and financial resources required and available with the number of girls that may possibly be reached.
- If good defaulter records are maintained, missed girls can be told to come to the health centre or next outreach session to catch up their vaccination, or they can be vaccinated the next time the health team goes to the school.
- Important strategies for missed girls include encouraging teachers to refer girls to the nearest health centre/outreach, reminder text messages to parents or guardians, and community announcements for vaccination days that will include HPV vaccine.

## CONSENT FOR VACCINATION

Consent processes for vaccination should be reviewed and determined by countries in accordance to national EPI policies. Specific policies and procedures for obtaining individual informed consent for HPV vaccines will need to consider local infrastructure and resources. For HPV vaccines, some countries have found that the introduction of a new or different consent procedure has led to suspicion that the HPV vaccine is experimental or risky. Therefore, the consent process needs to be carefully planned and implemented.

Consent procedures vary by country, and can include:

- formal, written consent (e.g. the caregiver signs a form either giving permission or refusing for vaccination of the child)
- verbal consent
- implied consent

As described previously (Key Resource page 21) WHO has developed a short resource document on consent approaches for vaccination of older children.<sup>1</sup>

When vaccination is carried out in schools, local or national school authorities normally authorize the intervention to take place at their premises. This authorization is needed for planning and implementing the vaccination sessions in schools. The same applies when community or traditional leaders are asked for permission for vaccination to be carried out in their communities. This authorization, however, does not imply informed consent by the individuals in that school or community. In a legal sense, school or local welfare or other community authorities do not have the capacity to consent to medical interventions on behalf of the children in their care. Exceptions, stipulated in local laws and regulations, may exist in defined, special situations.

When mandatory vaccination is established in relevant provisions in law, consent may not be required. If the mandatory nature of vaccination is based on policy, or other forms of soft law, informed consent needs to be obtained. Some countries allow individuals to express non-consent (opt-out) and obtain an exemption for mandatory vaccines.

For childhood vaccination, parental consent can be implied when a parent voluntarily brings the child to be vaccinated at a health clinic. However, older girls may not be accompanied by parents at the time of HPV vaccination, regardless of location. In these situations, implicit parental consent cannot be as easily assumed, and explicit written or verbal consent may require additional steps. Any explicit consenting or authorization process needs to be accounted for in the microplan and timeline established for HPV vaccine introduction.

Regardless of a country's informed consent policy, information and education to girls, their parents, teachers and the community should be given to allow understanding of the benefits and risks of HPV vaccination and to ensure acceptance. Effective communication strategies are described in the next chapter on communication and social mobilization.

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<sup>1</sup> [www.who.int/immunization/programmes\\_systems/policies\\_strategies/consent\\_note/en/](http://www.who.int/immunization/programmes_systems/policies_strategies/consent_note/en/)



## 6. COMMUNICATION AND SOCIAL MOBILIZATION



## DEVELOPING A COMMUNICATION PLAN

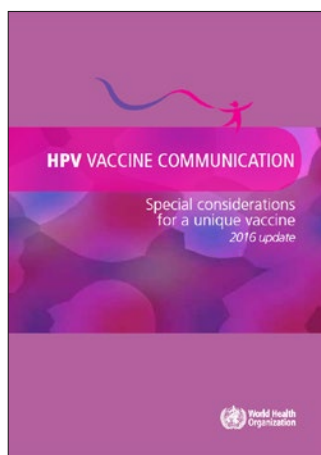
Increasing community awareness through timely, complete and appropriate communication is the key to successful and sustainable HPV vaccine introduction.

A comprehensive guide entitled *HPV vaccine communication: special considerations for a unique vaccine* (see Key Resource below) has been developed by WHO to assist countries to implement an effective communication strategy for sensitization and mobilization to improve HPV vaccine uptake. The introduction and continued delivery of any new vaccine requires a communication plan. Countries are encouraged to refer to this guide for detailed advice.

The basic elements of a communication plan include the following:

1. A communications team
2. Technical programme objective
3. Situation analysis
4. SMART<sup>1</sup> communication objectives
5. Target audiences
6. Messages for each audience
7. Strategies, activities, and channels to reach audiences
8. Branded materials
9. A crisis communication plan
10. Monitoring and evaluation plan
11. Work plan with budget (revised as required)

### KEY RESOURCE



### *HPV Vaccine Communication: Special considerations for a unique vaccine (updated in 2016)*

Communication is a key component of any successful public health programme, and an investment in communication for HPV vaccine is particularly important, given its unique qualities.

This document offers guidance in three main areas: (i) advice on basic communication planning and implementation for immunization; (ii) specific considerations for HPV vaccine; and (iii) crisis communication. It draws on the experiences from countries that have either introduced the vaccine nationally or conducted demonstration projects. It includes advice about cross-sectoral advocacy, team building and formative research; a description of the recommended target groups; the importance of careful planning so that communication reaches hard-to-reach girls; and advice on effective messaging, materials and channels.

[http://www.who.int/immunization/documents/WHO\\_IVB\\_16.02/en/](http://www.who.int/immunization/documents/WHO_IVB_16.02/en/)

<sup>1</sup> SMART Objectives are Specific, Measurable, Achievable, Relevant and Time bound.

## DEVELOPING KEY MESSAGES FOR HPV VACCINES

Creating effective messages is not easy. Accurate, technical, culturally appropriate, practical and motivational information must be conveyed in a way that can be easily understood by the different audiences at different times. The level of detail presented must be appropriate for each audience: girls, parents, teachers, health workers, and the wider community. Messages should be clear, simple and accurate. The actual wording of messages should consider culture, language, and literacy, and ensure a call to action.

Experience with HPV vaccine to date has provided some evidence about effective messaging. However each country is unique, and formative research, including focus group discussions and key informant interviews, may be needed to develop and test messages about HPV vaccination. Such exercises are part of the community engagement process and signal genuine care about addressing the views of target groups. For HPV vaccine, research can also help to pinpoint colloquial language; culturally-appropriate language and terminology for sometimes sensitive areas such as sexual behaviour and anatomy; and for preferred, trusted information sources and channels (e.g. public announcements, use of mobile phone text messaging (SMS) or social media).



### **Box 8. Examples of key messages for HPV vaccine acceptability**

- HPV vaccine for young girls protects them from cervical cancer later in life when they are grown women with families of their own.
- Cervical cancer affects the reproductive organs of women and is a leading cause of death among women of child bearing age.
- Girls should be vaccinated when they are young before exposure to HPV.
- You can protect your daughter and her future by getting her vaccinated.
- The vaccine is safe, causes no major side-effects, and will not harm a girl's ability to have children in the future.
- HPV vaccine is available free-of-charge at (location) (date, time).
- Most girls should be vaccinated twice, with 6 months (or indicate chosen schedule) between doses.
- The government supports HPV vaccination and has added it to the national immunization programme.

## IDENTIFYING THE AUDIENCES

Because HPV vaccine will be new, targeting an age group not normally included in the EPI schedule, and could have some potential sensitivities, it is important that communication messages reach every group that will have an interest in the vaccine. Each audience should be mapped out, and each will require specific messages – some requiring more information than others. For example, depending on literacy and culture, girls and their parents will require basic information about the vaccine, vaccination programme and schedule, using simple easy-to-understand language. However,

others in the community such as community and religious leaders, government officials, and health and education authorities may need more targeted messages to foster their understanding of the programme, the government's rationale for including HPV vaccine in the national immunization schedule, the vaccine safety and the benefit for girls.

School headmasters and teachers are also an important audience, especially if they have an active role in supporting vaccinations at school. Health workers will require the most detailed information as they may need to be convinced about the importance of HPV vaccine, and need to provide information and answer questions from parents, girls, and the community, as well as for their own understanding to be able to answer questions they may receive.

Professional organizations, cultural and religious organizations, politicians, and the media are also important audiences as they need to support vaccination of their communities.

## USING MULTIPLE CHANNELS AND OPPORTUNITIES FOR COMMUNICATION

It's important to use multiple channels to provide and reinforce messages.

Country experience has shown that parents' decisions are heavily influenced by receiving information from sources they trust - principally their families and close friends, local health workers, their teachers and religious leaders. Parents also like to receive information through interpersonal, direct communication and discussions.

Materials such as short "frequently asked questions" or simple brochures in locally understood languages may help reinforce verbal messages.

A variety of other activities and channels could be considered. These may include public media such as posters, billboards, and announcements in the community, at churches and mosques, or on the radio. In areas with access, television spots, mobile phone text messaging (SMS), and social media may be important and effective communication channels, particularly for young people.

A country example showing the range of communication activities used for HPV vaccination is presented below (see **Table 5**).

The timing of communication and social mobilization activities is critical to ensure there is a penetration of information to all audiences in good time prior to HPV vaccination. Each target audience may be different in the intensity and frequency required and this should be included in the communication plan. An example of the timing and frequency of HPV communication is provided in **Annex 3**.

Table 5. Example of a communication plan for HPV vaccines

AUDIENCE	MESSAGES	DELIVERED BY	ACTIVITIES	MATERIALS
Eligible girls	Basic facts about cervical cancer	Sub-county supervisors	Sensitization meeting	HPV leaflet
	Basic facts about the preventive HPV vaccine	Health workers Teachers	Distributing materials	
	Benefits of being vaccinated	Parents Mobilizers	Radio messages	
	Their role in HPV vaccination			
Parents	Facts about cervical cancer and prevention	District Health Team	Orientation sessions	HPV leaflet Radio messages
	Availability of preventive vaccine	Sub-county supervisors	Distributing materials	Articles in local media
	Facts about the vaccine	Health workers Teachers	Radio messages	
	Age-appropriate ways to discuss cervical cancer with children	Mobilizers	Publish information in local media Community film shows	
	Their role & responsibility			
School administration, School management and teachers	Facts about cervical cancer and prevention	District Health Team	Orientation sessions	HPV leaflet HPV guidebook
	Availability of preventive vaccine	School Management	Distributing materials	Radio messages
	Facts about the vaccine	Sub-county supervisors	Radio messages	Articles in local media
	Age-appropriate approaches to addressing cervical cancer with children	Health workers	Publish information in local media Community film shows	
	Their roles & responsibilities			
Community leaders	Burden of disease	District Health Team	Orientation sessions	HPV leaflet HPV guide
	Importance and benefits of prevention	Sub-county supervisors	Distributing materials	Radio messages
	Availability of preventive vaccine	Health workers	Radio messages	Articles in local media
	Facts about the vaccine		Publish information in local media	
	Key messages to help dispel misinformation		Community film shows	
	Their roles & responsibilities			

## RUMOURS AND CRISIS MANAGEMENT

Experience with HPV vaccine shows that communication crises are fairly common – and often due to rumours and misinformation. A good communication plan can avert these problems, and also help to manage them if a crisis emerges.

While HPV vaccines have an excellent safety profile, experience from some countries indicate that misperceptions about HPV vaccine risks can have serious consequences, and in some cases, has led to a complete halt to all HPV vaccination activities in the public sector.

Countries should ensure clear communication about the safety and common side effects of the vaccine, together with endorsement from trusted leaders. Communication helps build trust with the public. This involves including information on possible side effects in any education material or messaging used when communicating with parents and the community. Awareness among health workers and the public of possible adverse events will also reduce fear and misunderstanding and facilitate early recognition and treatment of side effects. It is very important to engage the media (through journalist briefings, information packages, etc.) prior to HPV vaccination, because if they are not well informed about the facts media can often amplify any rumours, leading to a larger crisis.

Countries should prepare a crisis communications plan to allow for a rapid effective response to AEFIs, anti-vaccine movements, and any allegation that can have a negative effect on public acceptance of HPV vaccines and trust in the immunization programme. Countries should have in place the basic elements of a crisis plan, which may include:

- An AEFI committee at different levels which can meet immediately to discuss an action plan;
- Identified, well-respected spokespersons at all levels;
- Clear channels of communication with various media;
- Engaging with credible opinion and traditional leaders to address misconceptions and rumours;
- Training of health workers on how to communicate with the public about AEFIs and safety concerns; and
- An AEFI action plan with specific roles for immunization programme partners.

WHO's document *HPV Vaccine Communication: Special Considerations for a unique vaccine* has been updated in 2016 to include the latest information and global experiences with managing HPV vaccine communication crises. See additional Key Resources below.



## KEY RESOURCES

### *WHO On-line e-Learning Course in Vaccine Safety*



WHO's Global Vaccine Safety group has developed an online e-learning course on Vaccine Safety basics to help health workers understand the origin and nature of adverse events, the importance of pharmacovigilance, and risk and crisis communication.

The content of this course has been compiled by international vaccine experts committed to the promotion of best practice in the implementation of immunization programmes worldwide. It includes a case-study on how a potential HPV vaccine crisis was averted (<http://vaccine-safety-training.org/c-introduction.html>).

For those who do not have constant internet access the e-learning course is available as a CD-ROM or downloadable PDF.

<http://vaccine-safety-training.org/home.html>

### *Vaccine Safety Events: Managing the Communication Response*



This manual developed by WHO's European Regional Office provides practical, informative strategies and tools to help plan and manage a communications response following a vaccine-related event in your local community, at a national level, or beyond. By reading this manual, you will learn how to use communications strategies and tools to increase public trust and confidence in vaccines, and to minimize the negative impact of any vaccine-related event.

[www.euro.who.int/\\_\\_data/assets/pdf\\_file/0007/187171/Vaccine-Safety-Events-managing-the-communications-response-final.pdf](http://www.euro.who.int/__data/assets/pdf_file/0007/187171/Vaccine-Safety-Events-managing-the-communications-response-final.pdf)

**Box 9. Summary: Communication planning and considerations for HPV vaccine\*****Communication is:**

- ✓ **A process.** People need time to change behaviours – to learn, absorb and confirm information, make a decision to act on it and encourage others to do the same.
- ✓ **About community engagement.** It's a conversation and not a lecture.
- ✓ **About equity** with plans to engage hard-to-reach populations.
- ✓ **An investment.** Effective communication activities will cost money and time. The return on investment is improved immunization coverage and better health for girls and women.
- ✓ **Imperfect.** Communication involves human beings, and we cannot predict what people will think or do in every situation.

**HPV vaccine is different:**

- ✓ **Start early.** Early planning can lead to on-time implementation. Begin communicating with communities about a month before the vaccine is introduced.
- ✓ **Build a cross-sectoral team.** HPV vaccine introduction involves immunization, education, cancer, sexual and reproductive health, adolescent health, youth, professional associations and other key members of civil society.
- ✓ **Conduct a situation analysis** including formative research if necessary. It's important to understand how different audiences understand and will respond to HPV vaccine.
- ✓ **Plan for a multi-year effort.** It will take time for HPV vaccine to "settle" in and be accepted as a part of a routine programme.
- ✓ **There will be concerns.** HPV vaccine is new in the country; it is targeted at adolescent girls; it may not seem like a priority, and there may be rumours about whether it's a "trial", its safety and about fertility.
- ✓ **Government endorsement is important for a successful programme.**
- ✓ **Identify and engage all groups that may have concerns.** Ensure advocacy plans for them.
- ✓ **Understand and plan for hard-to-reach girls.** Who and where are these girls? In the future, they may have the least access to cervical cancer screening even when it's available in the country.
- ✓ **Interpersonal communication from trusted influencers can have the most impact.** Train health workers and teachers to communicate effectively about HPV vaccine and ensure religious and community leaders understand and know how to promote it.
- ✓ **The first year will have some challenges.** It's a new programme and there will be bumps but...
- ✓ **High coverage can be achieved.** HPV vaccine will save lives. Communication has been key to high coverage in countries with successful programmes.

*\*From: HPV Vaccine Communication: Special considerations for a unique vaccine, WHO, updated 2016*



## 7. IMPLEMENTATION – TRAINING, SERVICE DELIVERY AND SUPERVISION



## TRAINING

Even though many aspects of HPV vaccine delivery are the same as for other established routine immunizations, health staff will need to receive specific training before implementing HPV vaccination. If prepared well, a two-day training should be sufficient to cover the necessary background information, operational issues and hands-on practice. Ideally, the training for HPV vaccine introduction would be included as a part of any regular annual or refresher training for health workers.

Linking training with an annual microplanning activity can also build efficiencies and allow for more integrated planning of vaccine delivery, especially if schools will be used as a location for vaccinations.

In cases where schools will have a role in the introduction of HPV vaccine, teachers and headmasters may also need a brief half-day orientation training in accordance to their specific tasks. Having school staff attend the first part of a planned health worker training may help to build trust and facilitate future collaboration.

For health workers, WHO has developed a training package of slide sets consisting of seven modules which can be downloaded from the WHO web site<sup>1</sup> and adapted by countries:

1. Introduction to HPV infection and cervical cancer
2. HPV vaccine attributes and storage conditions
3. HPV vaccine eligibility and contraindications
4. HPV vaccine administration
5. Recording and monitoring of HPV vaccine doses
6. Communicating about HPV with key stakeholders
7. Taking care of adolescent patients

Training materials need to be prepared (or translated) in the appropriate local language and in sufficient quantities. Summarized reference materials and job aids should be developed and given to the participants attending training so that they have information to refer to and to share with others when they return to their post. This is particularly important for cascade training.

Interactive, hands-on training, such as field visits, showing videos of correct practices, small group discussions, demonstrations and skills practices are generally more successful techniques for training adults than classroom lectures.

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<sup>1</sup> Essential Training Package for 2-dose schedule HPV vaccine introduction: [http://www.who.int/immunization/diseases/hpv/2dose\\_schedule/en/](http://www.who.int/immunization/diseases/hpv/2dose_schedule/en/)



**Box 10. Training for HPV vaccination for health workers should include the following:**

- Brief overview of cervical cancer morbidity and mortality and current strategy of the government for its prevention and control.
- Review of the rationale for adding HPV vaccine to the national immunization schedule
- Review of all relevant policies, such as population targeted, consent requirements, multi-dose vial policy, etc.
- Detail for the HPV vaccine delivery strategy chosen, definition of the target population, location of vaccinations, and frequency of delivery.
- Key messages for girls, parents and communities and the social mobilization plan.
- Conducting well-organized and efficient immunization sessions.
- Adverse events following immunization (AEFI) – how to prevent, detect, treat, and report.
- Instruction and practice on how to administer HPV vaccine, including schedule, dosage, storing and handling the vaccine, vaccine vial monitors (VVMs), co-administration with other vaccines, safe injection, and waste management.
- Data collection, record keeping and reporting forms for doses delivered, tally sheets, vaccine register, AEFI, etc.
- If applicable, seeking opportunities to integrate HPV vaccine delivery with other health or education interventions.
- Stock management of HPV vaccine supplies, including how to forecast supplies and wastage rates.
- Monitoring and supportive supervision plans.
- Microplanning (with schools, if applicable) to ensure that all communities, especially hard to reach, have access to vaccination services.
- Elaboration of the detailed timeline/chronogram for HPV vaccine introduction.

## SERVICE DELIVERY

### HOW TO ORGANIZE AN HPV VACCINATION SESSION

Vaccination sessions for HPV vaccine will be similar to those organized for infant immunizations. As with other vaccines, immunization sessions for HPV vaccine should have all the necessary supplies and materials for effective delivery. Supplies include chair and table, water and soap or hand sanitizer, safety boxes with closed lids, waste bags for garbage, and information, education and communication (IEC) materials. All forms and monitoring tools should be brought to every vaccination session, including the vaccination logbook or register, tally sheets, vaccination cards, and AEFI forms in case of immediate reactions.

In addition to following all the basic requirements for any injectable vaccine, a few additional steps before and after are required to properly administer HPV vaccine.



### Steps prior to HPV vaccine injection

1. Verify eligibility of the girl
2. Ensure name, address (if collected), and date of birth or age is recorded in vaccine register
3. Ensure girl understands purpose, benefit and risks of vaccination, as well as of not receiving the vaccine
4. If required, check written consent received
5. Verify girl assents to vaccination
6. Ensure no contraindications
7. Check vaccination card and determine if 1<sup>st</sup> or 2<sup>nd</sup> dose is due
8. Ensure girl is seated for vaccination
9. Administer vaccine following the procedures for safe injection (see section below)

### Steps after HPV vaccine injection

1. All girls are strongly advised to rest for at least 15 minutes after vaccination, in case they experience dizziness or any immediate untoward effects
2. Document dose received and date in vaccine register and vaccination card
3. Remind girl of need and date of next dose, if applicable
4. If all doses have been completed, return completed vaccination card to the girl for safe keeping
5. Should any adverse event occur, manage, document, and report according to established national AEFI guidelines

When HPV vaccination takes place in schools, teachers may be able to assist in mobilizing girls for vaccination, checking registers for eligibility, and providing support to health workers by recording information on vaccination cards and/or registers. A classroom in the school may also be a convenient enclosed space to conduct the vaccination session while minimizing disruptions to the rest of the school. **Figure 3** provides an example of the client flow for a school-based vaccination session.

### PRIVACY

If possible, it may be beneficial that actual vaccination is done privately, rather than in front of the whole group of girls. Fear of pain, or instances of fainting, may affect the larger group. This can cause mass psychogenic reactions and a crisis situation against HPV vaccination. Existence of social media nowadays has led to the rapid spread of fears beyond a single vaccination site or school.

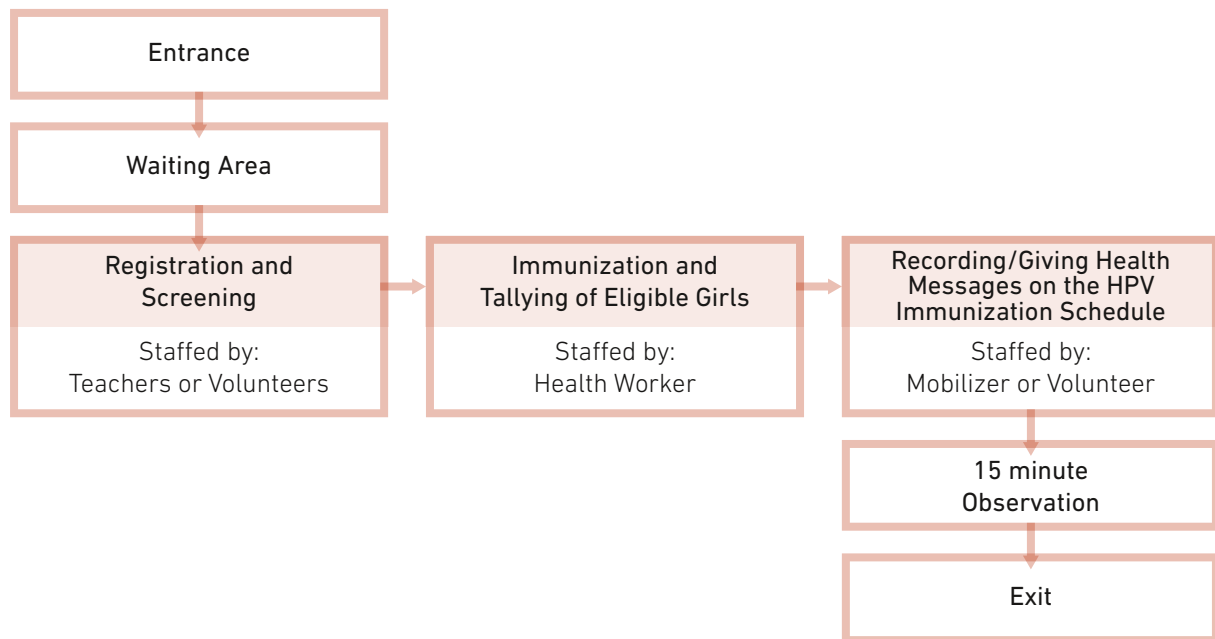
Practical suggestions to reduce fear and distress include:

- Use a screen for privacy
- Have girls wait outside the vaccination room
- Manage only small groups of girls at a time

Research studies<sup>2</sup> have documented that fear of HPV vaccination was promoted by witnessing the fear reactions of peers; perceived judgement by peers; lack of information or misinformation; and being vaccinated later in the day. Fear was moderated by procedural factors, the support of peers, appropriate knowledge, and nurses' distraction techniques or approach. Fear also affected acceptance of HPV vaccination.

<sup>2</sup> Bernard, D. et. al. *The domino effect: adolescent girls' response to human papillomavirus vaccination*. MJA, Vol. 194, No. 6, 2011. <http://sanevax.org/wp-content/uploads/2011/03/Domino-Effect2.pdf>

Figure 3. Client flow for school-based vaccinations – an example



### SAFE INJECTION PRACTICES

As with all other immunizations, HPV vaccine should be delivered with good technique and following the best practices for safe injections:

1. Always follow manufacturer recommendations for use, storage, and handling
2. To minimize risk of injury, prepare work area such that:
  - a. The vaccine administrator is placed between the girl and needles and sharp objects
  - b. Monitoring tools and safety boxes are easily accessible
  - c. Each vaccinator has a designated safety box and can see the entrance hole when discarding needle
3. Wash hands with soap and water and drip dry
4. Prepare each dose immediately before administering. Do not prepare several syringes in advance
5. Check the vial for condition, VVM status, and expiry date. Do not use if the colour of the VVM's inner square is the same colour or darker than the outer circle, or if packaging is punctured, torn, or damaged, or if vial contains particles or if there is discoloration
6. Use a new auto-disable (AD) syringe for each girl
7. Do not touch any part of the needle
8. Inject entire content of the syringe into the deltoid muscle of the upper arm using a perpendicular 90 degree angle
9. Discard the syringe and needle directly (no recapping) into a safety box immediately after administering the vaccine

10. Safety box should be a water-proof and tamper-proof container that is securely closed with only a small hole at the top large enough for syringe and needle to enter
11. Do not overfill the safety box. Close the container and seal the opening when the box is  $\frac{3}{4}$  full
12. Keep safety boxes in a dry, safe place until they can be safely disposed
13. Do not dispose of used syringe and needles in an open box or container

### ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)<sup>3</sup> MONITORING

An adverse event following immunization is any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the use of the vaccine. If not rapidly and effectively dealt with, AEFIs can undermine confidence in a vaccine and ultimately have dramatic consequences for immunization coverage and disease incidence.

Although an AEFI can be caused by the vaccine itself, reported AEFIs are more commonly either a coincident event that is not related to the vaccine, due to programmatic or human errors that compromise the vaccine quality, or allergic reactions to components in the vaccine.

AEFIs can be classified into 5 categories:

#### 1. Vaccine product-related reaction

- Caused or precipitated by inherent properties of the vaccine product

#### 2. Vaccine quality defect-related reaction

- Caused or precipitated by a vaccine due to one or more quality defects of the vaccine product, including the administration device, as provided by the manufacturer.

#### 3. Immunization error-related reaction

- Caused by inappropriate vaccine handling, prescribing or administration and that thus, by its nature, is preventable.

#### 4. Immunization anxiety-related reaction

- Arising from anxiety about the vaccination.

#### 5. Coincidental event

- Caused by something other than the vaccine product, immunization error or immunization anxiety.

Common HPV vaccine reactions which resolve spontaneously and rarely require treatment are:

- Redness, pain, swelling, or induration at injection site
- Fever
- Headache, myalgia, arthralgia
- Nausea, vomiting, diarrhea, abdominal pain
- Pruritis, rash, urticaria
- Syncope, dizziness

Serious adverse events are extremely rare. Anaphylaxis can be causally related to HPV vaccination and precautions should be taken to avoid vaccinating girls with previous allergic reactions to vaccine components. If anaphylaxis is suspected, the girl should be observed and immediately treated as needed, according to the established protocols of the EPI programme. Emergency kits to treat anaphylaxis should be always available when vaccination is provided.

<sup>3</sup> WHO, 2013. Causality assessment of an adverse event following immunization (AEFI): User manual for the revised WHO AEFI causality assessment classification. [http://www.who.int/vaccine\\_safety/publications/gvs\\_aefi/en/](http://www.who.int/vaccine_safety/publications/gvs_aefi/en/)

WHO produces a series of Information Sheets on the Observed Rate of Vaccine Reactions which are available on the web.<sup>4</sup> The Information Sheet on the Observed Rate of Vaccine Reactions for HPV vaccine is provided in **Annex 4**.



### **Box 11. HPV Vaccine and the Global Advisory Committee on Vaccine Safety (GACVS)**

The Global Advisory Committee on Vaccine Safety (GACVS) was established in 1999 to respond promptly, efficiently, and with scientific rigour to vaccine safety issues of potential global importance. The Committee provides independent, authoritative, scientific advice to WHO on vaccine safety issues of global or regional concern with the potential to affect in the short or long term national immunization programmes.

**On a regular basis, the GACVS has systematically reviewed and investigated safety concerns raised about HPV vaccines. To date, GACVS has not found any safety issue that would alter its recommendations for the use of the vaccine.**

Concerned about the persistence and public health harm caused by HPV vaccine safety issues based on anecdotal observations and reports in the absence of biological or epidemiological substantiation, in 2014 GACVS issued a statement summarizing their findings over six years. This summary statement, and all other HPV vaccine safety statements (most recent January 2016) and GACVS meeting reports are available at: [http://www.who.int/vaccine\\_safety/committee/topics/hpv/en/](http://www.who.int/vaccine_safety/committee/topics/hpv/en/)

The GACVS continues to closely monitor the safety of HPV vaccines.

### **Monitoring and reporting of AEFI**

Monitoring HPV vaccine safety is of particular importance because it is a new vaccine and is administered to an age group not previously targeted for vaccination in many countries. Groups opposed to vaccines for any reason may initiate or perpetuate rumours of vaccine safety and spurious associations with coincident adverse events to discourage HPV vaccination in the population. Because misinformation can be detrimental to vaccine acceptability and vaccination efforts, a robust AEFI monitoring infrastructure is essential to dispel rumours and demonstrate continued safety of HPV vaccines.

A system should be in place to facilitate prompt reporting and investigation of AEFIs. The National Regulatory Authority (NRA) and the National Immunization Technical Advisory Group (NITAG) should take a proactive role in investigation of reports of serious adverse events to verify any link to HPV vaccine and develop communication messages to address rumours. Clear procedures for what should be reported and how are necessary elements of any AEFI reporting system. Health workers should be trained on the recognition of adverse events, completion of the AEFI reporting form, and appropriate notification of supervisors and the district health officer, according to established protocols. Countries should ensure that HPV vaccine adverse event monitoring is fully incorporated within the national AEFI guidelines prior to national introduction.

**Annex 5** provides an example of an AEFI reporting form for HPV vaccine that can be adapted for country context as well as a generic reporting flow for the AEFI reporting form once completed.

<sup>4</sup> [http://www.who.int/vaccine\\_safety/initiative/tools/vaccinfosheets/en/](http://www.who.int/vaccine_safety/initiative/tools/vaccinfosheets/en/)

The WHO *Aid memoire for AEFI Investigation* and a sample AEFI investigation form can be found in Annex 6.

Detailed procedures for reporting AEFIs are described in the WHO *Global manual on surveillance of adverse events following immunization*, 2014.<sup>5</sup>

## SUPPORTIVE SUPERVISION

Once HPV vaccine is introduced, implementation should be periodically monitored through supportive supervision, which includes “on-the-job” training. Supportive supervision strengthens the capacities of health workers and improves performance; visits can be used to provide feedback, update health staff on this and other vaccinations, enhance motivation, and identify training needs.

Supervisor schedules and integrated checklist tools should be adapted to include HPV vaccine. Staff should be specifically asked about HPV vaccine coverage and any problems (supply or demand) that they face with this vaccine. Managers can refer to WHO’s *Training for Mid-Level Managers (MLM): Module 4 - Supportive Supervision*<sup>6</sup> to develop effective supportive supervision programmes and for a sample supervisory checklist that can be adapted to include HPV vaccine.



### Box 12. Supportive supervision:

- Encourages open, two-way communication;
- Builds team approaches that facilitate problem solving;
- Focuses on monitoring performance towards goals;
- Uses data for decision-making;
- Depends on regular follow-up with staff to ensure that new tasks are being implemented correctly.

***Supportive supervision is helping to make things work, rather than checking to see what is wrong.***

<sup>5</sup> [http://www.who.int/vaccine\\_safety/publications/aeft\\_surveillance/en/](http://www.who.int/vaccine_safety/publications/aeft_surveillance/en/)

<sup>6</sup> WHO Training for mid-level managers (MLM): Module 4 – Supportive Supervision, 2008. [http://www.who.int/immunization/documents/MLM\\_module4.pdf](http://www.who.int/immunization/documents/MLM_module4.pdf)



## 8. MONITORING AND EVALUATION



## MONITORING TOOLS

The main recording and reporting tools that are used for immunization should be adapted to include HPV vaccine. These are:

- Immunization register
- Tally sheet
- Immunization card (Home-based Record)
- Defaulter tracking system
- Stock record
- Integrated monthly report

This chapter provides brief highlights. More general information can be found in WHO's *Immunization in Practice: A Practical Guide for Health Staff, Module 6 – Monitoring and Surveillance*, 2015<sup>1</sup>.

Specifically for HPV vaccine, WHO has also developed a new resource -- *HPV Vaccine Coverage Monitoring Tool*<sup>2</sup> which explains in detail, according to different delivery strategies, how HPV vaccine recording and monitoring tools can be adapted. It includes examples of standardized forms and tables for all levels (service delivery, district, and national).

### IMMUNIZATION REGISTERS

Immunization registers record doses given to an individual and helps health workers keep track of each dose that has been administered and the completion of the vaccination series. The immunization register is the basis for tracking individual immunization status (should for example, the vaccination card be lost) and for tracking defaulters.

Depending on the HPV vaccination delivery strategy that is being used it may not always be possible to take the immunization register away from the health facility. In these circumstances it may be helpful to develop a separate HPV vaccination register or defaulter tracking system using duplicate vaccination cards, or use temporary register sheets which can be copied back into the main register after the outreach has been completed.

Each dose of HPV vaccine delivered to every eligible girl should be recorded against their name in the register. When used effectively and the records are organized in manner that facilitates identifying particular children, registers can be an additional tool for health workers to be aware of who has missed doses and allow for tracking of defaulters. An example is provided in **Annex 7**.

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<sup>1</sup> <http://www.who.int/immunization/documents/training/en/>

<sup>2</sup> WHO, to be published in 2017



**Box 13. Immunization registers should include the following data:**

- A unique identification number, if possible;
- Registration date (usually the date of the first visit);
- Name of the girl;
- Date of birth;
- Sex of the vaccine recipient (HPV vaccine is only given to girls);
- Name and mobile phone number of parent/guardian, if feasible, to facilitate reminders;
- Space to record date and dose administered (e.g., dose 1 or dose 2);
- Other data of relevance to the immunization programme (including adverse events).

## TALLY SHEETS

Tally sheets are the forms that health workers use to document an immunization session by making a record for every dose of vaccine given. Tally sheets should be used at all vaccination sessions whether at the health centre, fixed outreach, school, or conducted by mobile teams. Tally sheets are also useful in tracking both doses delivered and any vaccine doses wasted. An example of a tally sheet for HPV vaccine is provided in **Annex 8**.

It is recommended that the HPV vaccine tally sheet track the doses given by age (this is particularly important if using a school class or grade as the target population). As this might be new for some national immunization programmes, it is advised that health worker training prior to HPV vaccine introduction carefully review the proper method for using the HPV vaccine tally sheet. Supportive supervision visits should also monitor appropriate use and completion of the tally sheet to improve the quality of data reporting.

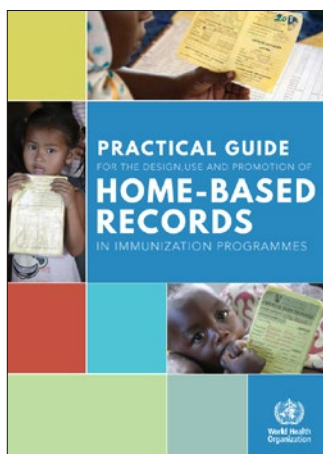
## IMMUNIZATION CARDS

Immunization or vaccination cards are an essential tool to track immunization history, and are easily adaptable for HPV vaccine. The vaccination card can:

- Enable health workers to determine which doses are due
- Serve as a reminder for the next visit/dose
- Facilitate coverage surveys
- Serve as documented proof of immunization status if required for school entry or for other reasons (i.e. later in life for cervical cancer screening)

While it is always desirable to have an immunization card that includes vaccination over a lifetime, it is recognized that many countries are using vaccination cards only for infant vaccination. In these cases, it will be necessary to create a new vaccination card for adolescent vaccinations that includes HPV. Even if HPV is the only vaccine currently given to this age group, it may be sensible to include options for other vaccines to be added (e.g. Td, dengue). (see **Annex 9** for an example HPV vaccination card and Key Resource below for an example of such a card that follows the life course).

For countries using schools as the HPV vaccination location, the vaccination card is often kept at the school until the series is completed, at which time the card is given to the girl for safe-keeping and documentation of completion of both doses of HPV vaccine.

**KEY RESOURCE***Practical guide for the design, use and promotion of home-based records in immunization programmes*

This document provides guidance to national immunization programmes on how to improve the design of home based records and how to promote their use among health workers and caregivers.

[http://www.who.int/immunization/monitoring\\_surveillance/routine/homebasedrecords/en/](http://www.who.int/immunization/monitoring_surveillance/routine/homebasedrecords/en/)

**TRACKING DOSES AND DEFAULTERS**

As with other vaccinations, it is important to follow-up eligible girls who fail to present for either the first or second dose of HPV vaccine. High levels of defaulting could be an indication of more systemic problems in the community, such as lack of confidence or trust in the vaccine, or in service delivery, such as stock outs. A system to track drop-outs is an integral part of the Reaching Every District (RED) or Community (REC) strategy.<sup>3</sup> The RED/REC approach can and should be used to ensure high coverage with HPV vaccine (**Box 14**).

**Box 14. Five “RED or REC” components to increase immunization coverage**

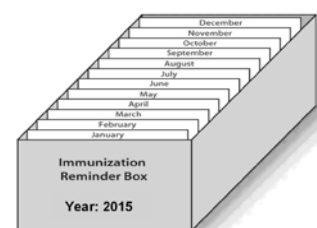
1. **Planning and management of resources** – better management of human and financial resources.
2. **Reaching target populations** – improving access to immunization services by all.
3. **Linking services with communities** – partnering with communities to promote and deliver services
4. **Supportive supervision** – regular on-site teaching, feedback and follow-up with health staff.
5. **Monitoring for action** – using tools and providing feedback for continuous self-assessment and improvement.

Two common ways of monitoring and follow-up of defaulters are the immunization registers and reminder cards (sometimes called “Tickler Boxes”).

- (i) **Using the immunization register** – regularly review the immunization register to identify girls who may have failed to receive their second dose of HPV vaccine when due.

<sup>3</sup> AFRO RED Guide (2008) [http://www.who.int/immunization/programmes\\_systems/service\\_delivery/red/en/](http://www.who.int/immunization/programmes_systems/service_delivery/red/en/) Immunization in Practice: A Practical Guide for Health Staff, Module 4 –Microplanning for Reaching Every Community (2015) [http://www.who.int/immunization/documents/IIP2015\\_Module4.pdf?ua=1](http://www.who.int/immunization/documents/IIP2015_Module4.pdf?ua=1)

- (ii) **Reminder cards** – another way to identify “drop-outs or defaulters” is to make copies of the vaccination card for HPV vaccine. File a copy of the card in a box with dividers by month as shown below. The reminder card is put in the month that the missed dose of vaccine is due. Health workers can use community messaging, reminders to parents, mobile phone texts, or other mechanisms to send reminders of the need for attending to receive the missed vaccine dose. Tracking every month will provide consistency and make the exercise a regular part of the work of the health centre staff.



- (iii) **Electronic immunization registries (EIRs)** – more and more countries will be developing and implementing computerized registries that include records for each child with personal information as well as vaccination data. EIRs allow automating the generation of listings of children who are due for a vaccine or who have missed a dose, as well as sending recall/reminders by phone, email or letters directly from the EIR to consenting users.

## MONTHLY REPORT

HPV vaccine immunization data should be collected on a monthly basis at each level of the health system, as is done for all other vaccines on the national immunization schedule. This may be done in a form specifically tracking HPV immunization, or as part of the integrated monthly report. The integrated monthly report contains critical data on most of the components of the immunization system in summary format for both easy recording and easy tracking. It is a valuable tool for management of the programme’s achievements and to monitor progress throughout the year. The integrated monthly report should be adapted when HPV vaccine is added to the national immunization schedule. Annex 10 provides an example of a stand-alone monthly report for HPV vaccination. Additional examples of integrated monthly reports, illustrating the summary nature of the data for all vaccines administered in various formats, can be found in the **HPV Vaccine Coverage Monitoring Tool**<sup>4</sup>.

If the HPV vaccine delivery strategy only provides vaccination periodically (i.e. every 6 months or annually; not continuously throughout the year) then “zero” reporting will be necessary for the months when HPV vaccine is not given.

## COVERAGE MONITORING

Calculating HPV vaccine coverage is necessary for monitoring the impact of vaccine on a population, as well as for evaluating the performance of a vaccine programme toward meeting objectives. As with other EPI vaccines, administrative coverage can be supplemented by coverage surveys (see coverage surveys below).

Since HPV vaccination is recommended as a 2-dose series of vaccines administered 6 months apart to 9-14 year-old girls, HPV vaccine coverage monitoring requires collection of coverage data by dose and by age. At a minimum, the girl’s date of birth or age, date of vaccine administration, and dose number should be recorded each time a vaccine is administered.

A coverage monitoring wall chart for HPV vaccination should be maintained and displayed in the health facility. This chart should include the target population of girls at the health facility or catchment area, and record the number of girls vaccinated per month, per dose, over time, until the

<sup>4</sup> WHO, to be published in 2017.

target is reached. If campaign-style delivery is used, then setting up the charts showing two time points can be used to provide a visual record of the administrative coverage (per outreach per dose).

### WHO/UNICEF JOINT REPORTING FORM ON IMMUNIZATION

National immunization programmes provide HPV vaccination to different age groups of young adolescent girls or persons. For international comparison of two-dose HPV vaccine coverage and for calculating regional and global coverage for girls by a certain age, all countries are requested to report the number of HPV doses administered by single year of age after national introduction of HPV vaccine to the international community via the WHO/UNICEF Joint Reporting Form on Immunization (JRF). This form is commonly used for all other routine immunizations and has been adapted to accommodate HPV vaccine (see **Table 6**).

**Table 6.** Excerpt from WHO/UNICEF Joint Reporting Form for HPV vaccine doses administered

VACCINE ADMINISTERED (AGE IN YEARS)	HPV VACCINE DOSES ADMINISTERED: [YEAR]		
	FEMALES		
	A. 1ST DOSE	B. 2D DOSE	C. 3D DOSE*
9			
10			
11			
12			
13			
14			
15+			
unknown age			

\*WHO recommends a 2-dose schedule for girls <15 years of age (Position Paper, Oct 2014). If a 2-dose schedule was used, please leave Column C blank.

**Note:** 3<sup>rd</sup> dose reporting only required for years prior to 2015, when the WHO recommended schedule for HPV vaccine was three doses. Some countries are continuing to use a three dose schedule, particularly if they are targeting girls >15 years of age.

Adapted from: WHO/UNICEF Joint Reporting Form, available at: [http://www.who.int/immunization/monitoring\\_surveillance/routine/reporting/en/](http://www.who.int/immunization/monitoring_surveillance/routine/reporting/en/)

## EVALUATION TOOLS

WHO has adapted the common evaluation tools so that they may be used for HPV vaccination. These tools measure similar outcomes of programme performance as conducted for other new vaccine introductions, but are modified to accommodate several unique features of HPV vaccine delivery.

### POST-INTRODUCTION EVALUATION (PIE)

Global experience with the introduction of new vaccines is now very extensive, and most countries have introduced at least one or more new vaccines in the last 10 years. For these reasons, WHO **no longer** recommends that all countries should conduct a post-introduction evaluation (PIE) 6-12 months following national introduction. More simply, the WHO recommendation is now to combine

the assessment of any new vaccine introduction with the next scheduled EPI Programme Review or other evaluation opportunity.

Nevertheless, given the uniqueness of HPV vaccine, some countries may still wish to conduct a PIE or a smaller scale assessment to evaluate the impact of the HPV vaccine introduction on the country's immunization programme and to rapidly identify problems needing corrective action that are the result of the introduction or that pre-existed.

To assist, WHO has developed a user-friendly PIE tool for assessing the introduction and implementation of HPV vaccination, which includes sample questionnaires and checklists that countries can adapt. Special components deal with involvement of schools and teachers, as well as for more intensive community sensitization and mobilization activities. Copies of the HPV PIE Tool are available from WHO's Department of Immunization, Vaccines & Biologicals (Contact: [vaccines@who.int](mailto:vaccines@who.int)).

### EPI PROGRAMME REVIEWS

EPI programme reviews are undertaken every three to five years and should be adapted to include HPV vaccine once it has been introduced.

WHO has recently revised its methodology for conducting EPI Reviews which recommends integrating immunization-related programme assessments, where feasible, in order to promote efficiency. If an HPV component will be integrated with the EPI Review, the main objectives and critical knowledge gaps regarding HPV introduction should be considered in the Desk Review stage so that these issues can be addressed through specific lines of questioning included in the review tools.

Additional modifications may be required as well, such as interviews with stakeholders or partners concerned specifically with HPV vaccine, and visiting additional sites, such as schools, if applicable.

Copies of the EPI Comprehensive Programme Review methodology are available from WHO's Department of Immunization, Vaccines & Biologicals (Contact: [vaccines@who.int](mailto:vaccines@who.int))

### VACCINATION COVERAGE SURVEYS

WHO recommends that national coverage surveys include HPV only when at least a full year of HPV vaccine introduction has occurred (to ensure all eligible girls for that year have the opportunity to complete the 2-dose series prior to the conduct of the survey). National coverage surveys are useful to validate administrative data reported throughout the year and allow for comparisons with coverage achieved in other countries.

WHO has recently adapted the vaccination cluster coverage survey manual and it now includes guidance on how to measure HPV vaccine coverage. Even though HPV vaccine delivery strategies may vary, it is recommended that accurate and precise estimates of HPV vaccine coverage be obtained by a certain age, and that if information on coverage by strategy is to be measured, queries about the strategy used to reach the girl and/or oversampling special groups be included. These considerations will help to accommodate sampling issues and hard-to-reach sub-populations (such as out-of-school girls). The working draft of the new WHO **Vaccination Cluster Coverage Survey Manual** is available at [http://www.who.int/immunization/monitoring\\_surveillance/routine/coverage/en/index2.html](http://www.who.int/immunization/monitoring_surveillance/routine/coverage/en/index2.html)



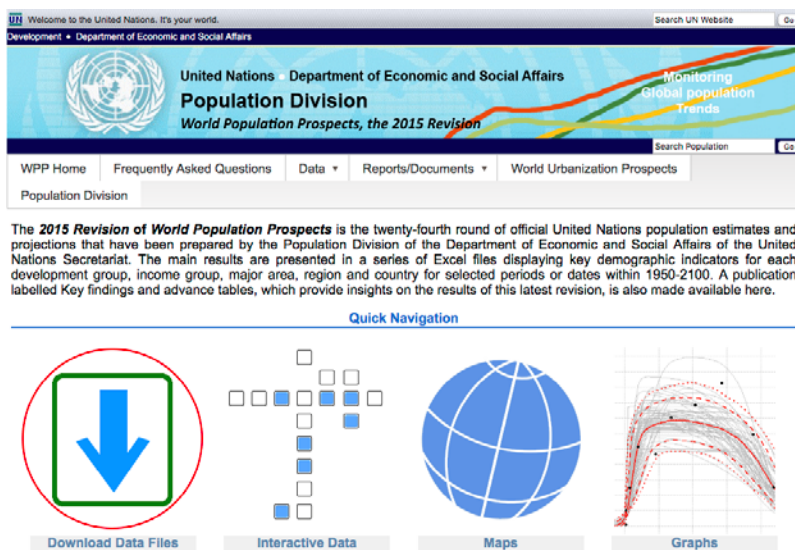
# ANNEXES



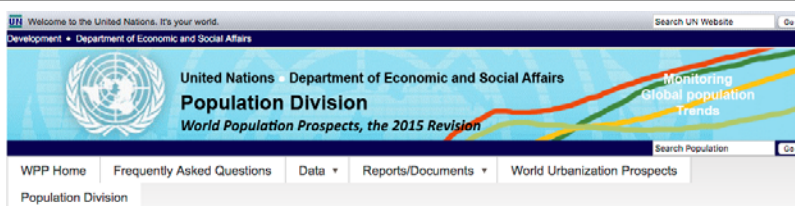
# ANNEX 1. UN POPULATION DIVISION – FEMALE POPULATION BY SINGLE AGE, MAJOR AREA, REGION AND COUNTRY, ANNUAL ESTIMATES 1950-2100

Annual population estimates for single age cohorts for females (and also males) by country are available from the United Nations Population Division website: <https://esa.un.org/unpd/wpp/>. Single year of age data can be downloaded from tables in Excel format under “Data”, subheading “Interpolated indicators”. The UN Population estimates are revised every two years; the next revision will be in 2017.

1. On the UN Population Division home page, go to “Download Data Files”



2. Under Major topic/Special groupings, select “Interpolated indicators”



3. Select the subgroup in which you are interested (e.g. Age composition: Annual Population by Age - Female)

Sub Group	Files (click to download)	Description
Age composition	<a href="#">Annual Population by Age - Both Sexes (XLS, 65.74 MB)</a>	Annual population by single age - Both Sexes. De facto population as of 1 July of the year indicated classified by single age (0, 1, 2, ..., 99, 100+). Data are presented in thousands.
Age composition	<a href="#">Annual Population by Age - Male (XLS, 65.7 MB)</a>	Annual population by single age - Male. De facto population as of 1 July of the year indicated classified by single age (0, 1, 2, ..., 99, 100+). Data are presented in thousands.
Age composition	<a href="#">Annual Population by Age - Female (XLS, 65.69 MB)</a>	Annual population by single age - Female. De facto population as of 1 July of the year indicated classified by single age (0, 1, 2, ..., 99, 100+). Data are presented in thousands.
Summary	<a href="#">Annual Demographic</a>	Annually interpolated demographic indicators.

4. Download Excel file and filter for the year and country you are looking for.

United Nations Population Division Department of Economic and Social Affairs World Population Prospects: The 2015 Revision File INT3-3: Female population by single age, major area, region and country, annually for 1950-2100 (thousands) Estimates, 1950 - 2015 POPDB/WPP/Rev2015/INT3-3 July 2015 - Copyright © 2015 by United Nations. All rights reserved Suggested citation: United Nations, Department of Economic and Social Affairs, Population Division (2015). World Population Prospects: The 2015 Revision, DVD Edition.																				
17	18	19	20	21	22	23	Female population by age (thousands)													
							0	1	2	3	4	5	6	7	8	9	10	11	12	13
88	146	Estimates	World		900	2015	63 077	65 441	64 697	64 211	63 561	62 884	62 218	61 555	60 914	60 292	59 707	59 173	58 665	58 166
149	132	Estimates	More developed regions	a	901	2015	6 465	6 631	6 734	6 787	6 826	6 828	6 806	6 767	6 716	6 658	6 597	6 535	6 489	6 487
215	198	Estimates	Less developed regions	b	902	2015	60 292	60 860	60 123	57 414	56 734	56 066	55 411	54 791	54 198	53 634	53 110	52 638	52 171	51 692
281	264	Estimates	Least developed countries	c	941	2015	14 337	14 035	13 750	13 481	13 226	12 981	12 746	12 524	12 302	12 072	11 854	11 641	11 413	11 181
347	330	Estimates	Less developed regions, excluding least developed countries	d	934	2015	45 255	44 815	44 373	43 903	43 499	43 075	42 665	42 274	41 905	41 562	41 256	40 987	40 757	40 529
413	396	Estimates	Less developed regions, excluding China	e	948	2015	51 596	50 919	50 273	49 665	49 083	48 495	47 949	47 422	46 916	46 426	45 949	45 486	45 034	44 582
479	462	Estimates	High-income countries	f	1503	2015	7 784	7 896	7 970	8 012	8 028	8 017	7 990	7 950	7 907	7 867	7 820	7 780	7 732	7 689
545	528	Estimates	Medium-income countries	e	1517	2015	47 771	47 309	46 848	46 360	45 845	45 361	44 975	44 607	44 278	43 913	43 583	43 290	43 024	42 741
611	594	Estimates	Upper-middle-income countries	e	1502	2015	16 756	16 618	16 468	16 312	16 153	15 994	15 841	15 697	15 565	15 440	15 344	15 241	15 180	15 128
677	660	Estimates	Lower-middle-income countries	e	1521	2015	31 015	30 691	30 379	30 079	29 780	29 507	29 234	28 970	28 713	28 463	28 219	27 979	27 744	27 515
743	726	Estimates	Low-income countries	e	1500	2015	10 499	10 253	10 015	9 784	9 558	9 341	9 127	8 917	8 711	8 507	8 307	8 109	7 909	7 702
809	792	Estimates	Sub-Saharan Africa	f	947	2015	16 369	15 939	15 520	15 111	14 712	14 323	13 942	13 568	13 202	12 843	12 491	12 149	11 805	11 455
875	858	Estimates	AFRICA		963	2015	19 262	18 743	18 221	17 716	17 227	16 754	16 296	15 852	15 424	14 991	14 573	14 159	13 746	13 334
941	924	Estimates	Eastern Africa		910	2015	6 658	6 503	6 352	6 206	6 063	5 924	5 787	5 652	5 520	5 388	5 258	5 130	4 999	4 880
1007	990	Estimates	Burundi		108	2015	220	213	205	197	189	181	173	165	157	149	143	136	129	
1073	1056	Estimates	Comoros		174	2015	12	12	12	11	11	11	11	10	10	10	9	9	9	
1139	1122	Estimates	Djibouti		262	2015	10	10	10	10	10	10	10	9	9	9	9	9	9	
1205	1188	Estimates	Eritrea		232	2015	79	80	80	79	78	77	75	73	71	69	67	64	62	
1271	1254	Estimates	Ethiopia		231	2015	1 502	1 465	1 430	1 410	1 389	1 372	1 357	1 345	1 333	1 323	1 313	1 303	1 296	1 271
1337	1320	Estimates	Kenya		404	2015	731	722	712	700	688	675	660	645	630	615	597	580	564	
1403	1386	Estimates	Madagascar		490	2015	394	382	372	362	353	345	337	330	323	317	311	306	300	295
1469	1452	Estimates	Mali		454	2015	300	297	293	288	282	276	268	260	252	244	236	227	219	
1535	1518	Estimates	Mauritius	1	480	2015	7	7	7	7	7	7	8	8	8	9	9	9	10	
1601	1584	Estimates	Mauritius		115	2015	3	3	4	4	4	4	4	3	3	3	3	3	3	
1667	1650	Estimates	Mozambique		508	2015	505	491	477	465	453	441	430	418	408	397	387	376	366	354
1733	1716	Estimates	Raionon		638	2015	6	6	6	6	6	6	7	7	7	7	7	7	7	
1799	1782	Estimates	Reunion		646	2015	163	168	170	172	172	170	168	165	162	157	153	147	142	138
1865	1848	Estimates	Seychelles		890	2015	1	1	1	1	1	1	1	1	1	1	1	1	1	
1931	1914	Estimates	Somalia		708	2015	207	201	196	190	184	178	172	166	160	154	148	143	138	134
1997	1980	Estimates	South Sudan		728	2015	203	198	193	188	183	178	174	170	165	161	157	154	150	147
2063	2046	Estimates	Uganda		800	2015	785	742	720	699	678	657	637	617	596	576	556	542	524	505
2129	2112	Estimates	United Republic of Tanzania	2	834	2015	992	958	927	898	870	844	819	795	771	748	727	706	683	656
2195	2178	Estimates	Zambia		894	2015	295	289	283	276	269	262	255	247	240	232	224	217	209	202
2261	2244	Estimates	Zimbabwe		716	2015	262	256	250	243	236	229	222	215	208	201	194	186	182	178
2327	2310	Estimates	Middle Africa		911	2015	2 838	2 745	2 656	2 571	2 489	2 410	2 335	2 262	2 192	2 124	2 058	1 995	1 931	1 866
2393	2376	Estimates	Angola		24	2015	503	485	468	452	436	421	406	392	378	364	351	339	326	314

[http://esa.un.org/wpp/Excel-Data/EXCEL\\_FILES/5\\_Interpolated/WPP2012\\_INT\\_F03\\_3\\_POPULATION\\_BY\\_AGE\\_ANNUAL\\_FEMALE.XLS](http://esa.un.org/wpp/Excel-Data/EXCEL_FILES/5_Interpolated/WPP2012_INT_F03_3_POPULATION_BY_AGE_ANNUAL_FEMALE.XLS)

## ANNEX 2. HOW TO PERFORM A SHAKE TEST

HPV vaccine should never be frozen; freezing damages the vaccine. The shake test is used to test a vial that has been suspected of freezing, to see if the vaccine has been damaged by freezing. The below table describes how to perform the shake test.

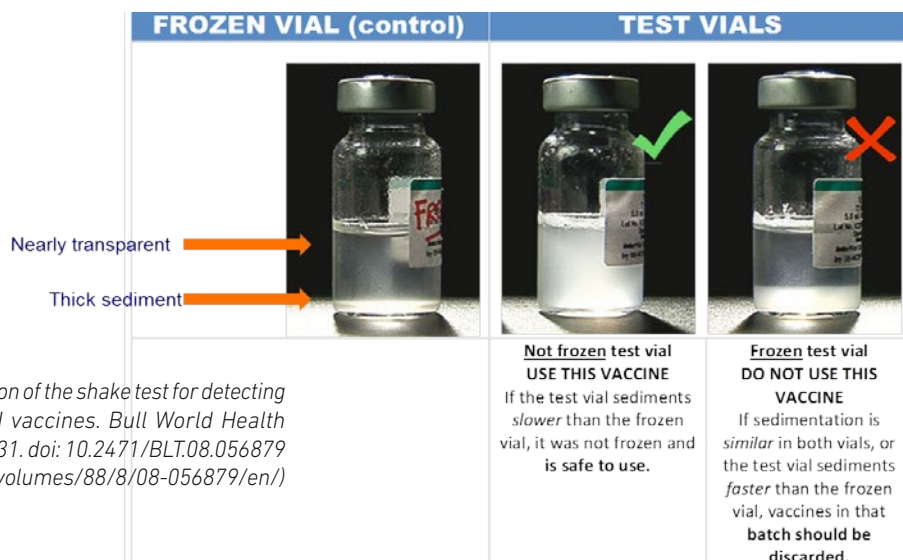
**How to conduct a shake test.** This protocol must not be altered. There is only one correct way to conduct a Shake Test.

**When to conduct a shake test.** The test procedure described below should be conducted on all suspect batches. In the case of international arrivals, the shake test should be conducted on a random sample of vaccine. However, if there is more than one lot in the shipment, the random sample must include a vial taken from each and every lot.

1. Take a vial of vaccine of the same type and batch number as the vaccine you want to test, and made by the same manufacturer.
2. Clearly mark the vial as "FROZEN."
3. Freeze the vial in a freezer or freezing compartment of a refrigerator until the contents are completely solid.
4. Let it thaw. Do **NOT** heat it!
5. Take your "TEST" vial from the batch that you suspect has been frozen.
6. Hold the "FROZEN" vial and the "TEST" vial together in one hand.
7. Shake both vials vigorously for 10–15 seconds.
8. Place both vials on a flat surface side-by-side and start continuous observation of the vials until the test is finished.

*(NOTE: If the vials have large labels that conceal the vial contents, turn both vials upside down and observe sedimentation in the neck of the vial.)*

Use an adequate source of light to compare the sedimentation rates between vials.	
IF...	
9. The TEST vial sediments slower than the FROZEN vial,	10. Sedimentation is similar in both vials
<b>THEN...</b>	<b>OR</b>
	The TEST vial sediments faster than the FROZEN vial
	<b>THEN...</b>
11. Use the vaccine batch.	11. <b>Vaccine damaged: DO NOT USE.</b> Notify your supervisor. Set aside all affected vaccine in a container marked "DAMAGED VACCINE FOR DISPOSAL– DO NOT USE"
	12. Discard all affected vaccine once you have received permission to do so.
	13. Fill in the Loss/Adjustment Form.



*(Source: Kartoglu et al. Validation of the shake test for detecting freeze damage to adsorbed vaccines. Bull World Health Organ. 2010 Aug 1;88(8):624-31. doi: 10.2471/BLT.08.056879 http://www.who.int/bulletin/volumes/88/8/08-056879/en/)*

## ANNEX 3. TIMING AND FREQUENCY FOR HPV VACCINE COMMUNICATIONS – A COUNTRY EXAMPLE

TIMING	ACTIVITY	FREQUENCY
At least two weeks prior to vaccinations	Billboards/posters placed at the district centre and in each community	Posters can be put up when HPV vaccinations are starting, and should remain until the second dose is complete.
	Messages broadcast on the <b>district</b> radio station	Messages should be broadcast on district radio for two to three weeks prior to each dose.
	Messages broadcast on the <b>community</b> radio station	Messages should be broadcast on the local radio station at least two weeks before vaccination, and two or three times per week for two weeks in each community prior to each dose.
At least one week prior to vaccinations	Parent meetings held at the school or in the community	One parent meeting should be held in each community at least one week before dose 1.
	Girls' meetings or information sessions held at the school or in the community	One group discussion or meeting can be held in each school or health facility at least one week before dose 1.
	Messages broadcast on the radio	Messages should be broadcast on the radio twice a day during the week before each dose (local, district, and national radio stations can be utilized).
	Banners and posters placed at the school and health facility	Banners and posters should be put up at identified places in each school or health facility at least one week before each dose.
	Leaflets and information about when vaccination will take place and location of vaccination sites	For each dose, girls and parents should be informed in advance of the date of vaccination and any follow-up vaccination activities that may occur for girls who missed doses.
Day of vaccinations	Provincial or regional meeting held to launch vaccination	A provincial or regional launch meeting can be held on the day of vaccination, attended by provincial/ regional and district staff.
	District meeting held to launch vaccination	A district launch meeting can be held at the district health center, district education department, district authority, or district IEC center, attended by heads of community health centers.
	Current information on vaccination progress broadcast on the community loudspeaker	Updated information should be broadcast twice in each community (on and after vaccination day) at the start of a new HPV vaccination programme.
	Leaflets and information provided at vaccination sites	Girls and parents should be given basic information about the vaccine and HPV, when the next dose should be given and any follow up vaccination activities that may occur for girls who missed doses.

## ANNEX 4. OBSERVED RATE OF VACCINE REACTIONS – HPV VACCINE



World Health  
Organization

Global Vaccine Safety,  
Immunization, Vaccines and Biologicals  
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### INFORMATION SHEET OBSERVED RATE OF VACCINE REACTIONS *HUMAN PAPILLOMA VIRUS VACCINE*

June 2012

#### The Vaccines

Currently available HPV vaccines are a recombinant viral protein vaccine containing highly purified virus-like particles (VLP) which are the protein shells of the HPV virus (major capsid protein L1) formed by recombinant DNA techniques. The VLP contain no viral DNA. Thus, they cannot infect cells, reproduce or cause disease. The VLP for each virus genotype are purified and then adsorbed onto an adjuvant.

The available vaccines differ in the number of HPV genotypes that they contain, the way that they are manufactured and the adjuvant that they contain. Both Bivalent and Quadrivalent vaccines are highly immunogenic and prevent primary infection with the HPV genotypes and prevent CIN 2/3 adenocarcinoma. Pre-licensure trials indicate a broadly similar safety profile for minor and serious adverse events for each of the vaccines. Post-licensure surveillance data concerning the safety profiles for each vaccine have detected no safety issues to date (as at November 2011) except rare reports of anaphylaxis.

#### Types of vaccines

	Vaccine antigens	Excipients
Quadrivalent	VLP from genotypes 6, 11, 16, 18	Produced in recombinant <i>S. Cerevisiae</i> culture. Aluminum hydroxyphosphate, Polysorbate 80, sodium borate and L Histidine
Bivalent	VLP from genotypes 16, 18	Produced in recombinant Baculovirus expression vector system. Aluminum hydroxide plus deacylated monophosphoryl Lipid A used as an adjuvant (AS04)

#### Adverse events

##### Mild adverse events

###### Local adverse events

Injection site pain is very common, having been reported in up to 80% of vaccinees for Bivalent (EMEA CHMP, 2007) and Quadrivalent vaccine (Markowitz et al., 2007). Severe pains (spontaneous pain or pain that prevented normal activity) was reported for approximately 6% (EMEA CHMP, 2007) of vaccinees. In pre-licensure placebo controlled clinical trials using the Quadrivalent vaccine, injection site reactions consisted of pain (84%) erythema (up to 25%) and swelling (25%), with pain occurring more commonly than in the placebo groups - both for saline only placebo (pain - 49%) and aluminium placebo (pain-75%). Local adverse reactions following Bivalent HPV vaccine were similar with 78% of vaccine recipients experiencing injection site pain compared with 52% who received the adjuvant alone or 59% who received Hepatitis A vaccine. In a trial comparing the two HPV vaccines in over 1,000 women aged 18 to 45, local reactions occurred more frequently with Bivalent than Quadrivalent vaccine. Injection site reactions included pain (92.9% Bivalent, 71.6% Quadrivalent), redness (44.3% Bivalent, 25.6% Quadrivalent) and swelling (36.5% Bivalent, 21.8% Quadrivalent) (Einstein et al, 2009).

###### Systemic adverse events

In clinical trials prior to licensure of the Quadrivalent vaccine, systemic adverse events were monitored for the first 15 days post vaccination. The only adverse event reported that occurred in greater than 1% of vaccines and occurred more frequently than placebo was pyrexia (10.1 versus 8.4% according to EMEA CHMP (2006), respectively). A number of other systemic adverse events, of minor nature were reported, but these occurred with an occurrence less than a 0.5% difference in the vaccinated group. Mild systemic adverse events possibly related to vaccination included headache, dizziness, myalgia, arthralgia, and gastrointestinal symptoms (nausea, vomiting abdominal pain). In a direct comparison of the Bivalent and Quadrivalent vaccines, systemic reactions were reported at comparable rates, with the exception of fatigue [49.8% (95% CI: 45.5-54.2) vs. 39.8% (35.6-44.1)] and myalgia [27.6% (95% CI: 23.8-31.6) vs. 19.6% (16.3-23.3)], which were reported more frequently amongst recipients of the Bivalent vaccine (Einstein et al., 2009).

### Severe adverse events

In pre-licensure trials, no severe adverse events attributable to the vaccine were recorded for either the Quadrivalent or Bivalent vaccine. Post-licensure clinical trials have included a randomized comparative cohort study on the safety of the Quadrivalent and Bivalent vaccines in 18-45 year old women. Systemic adverse events were monitored for 7 days and 30 days post vaccination. No clinically relevant differences were seen between the vaccinated groups (Quadrivalent vs Bivalent) with regard to new onset chronic disease which also included new onset autoimmune disease (Einstein MH et al., 2009). Follow-up of this cohort 18 months after the last dose of HPV vaccine (at 24 months) were similar between groups (Einstein MH et al., 2011).

*HPV vaccine and post-marketing surveillance.* As of September 15, 2011, approximately 40 million doses of Quadrivalent vaccine were distributed in the U.S. and VAERS received a total of 20,096 reports of adverse events following Quadrivalent vaccination: 19,075 reports among females and 569 reports for males, of which 504 reports were received after the vaccine was licensed for males in October 2009. Of the total number of reports, 92% were considered to be non-serious, and 8% were considered serious (VAERS 2011). Analysis of the currently available reports has not shown an excessive number of serious or unexpected adverse events (Slade et al., 2009). In particular, further investigation of case reports of Guillain-Barré syndrome, blood clots, and deaths have not revealed any pattern suggesting a causal association with vaccination. Analysis of conditions of interest arising among vaccinated and unvaccinated women using the Vaccine Safety Data link was generally reassuring. A non-significant excess of deep vein thrombosis was observed among women who had other risk factors. One vaccine-associated case of anaphylaxis was observed, with an overall rate of one per 1.7 million doses (95% CI 0.04, 9.3) (Gee et al., 2011).

In Australia, over 6 million doses of Quadrivalent vaccine have been used (as of June 2010) with 1534 adverse events reported (Therapeutic Goods Administration, 2008). These reports have included 16 reports of anaphylaxis which met the Brighton case definition for anaphylaxis (Rüggeberg J et al., 2007), and 133 reports of urticarial reactions (or hives). The current estimated rate of anaphylaxis based on doses given in Australia is 2.6 per million. The rate of anaphylaxis following Quadrivalent vaccine based on data from Vaccine Safety Data link in this study was 1.7 cases per million (Gee et al., 2011). The rates for anaphylaxis for other vaccines given to children and adolescents range from 0 to 3.5 per million doses in international studies which have used different case definitions for anaphylaxis (Bohkle et al., 2003).

In the United Kingdom, the Commission on Human Medicines (CHM) considered the MHRA's safety review of Bivalent vaccine and concluded that no serious new risks have been identified during its extensive use in the UK over 2 years, and that the balance of its benefits and risks remains positive. Similarly reassuring data on Bivalent vaccine was obtained in Italy (Gasparini, 2011), Malaysia (ADRAC Bulletin, 2011), and the Netherlands (van Klooster et al., 2011).

### Other safety issues

*HPV vaccine in combination with other vaccines.* Assessment of concomitant use of the Quadrivalent vaccine and recombinant Hepatitis B vaccine showed no increase in adverse events (Reisinger et al., 2010). Concomitant use of the Bivalent vaccine with combined diphtheria-tetanus-acellular pertussis-inactivated poliovirus vaccine to girls and young women. was generally well tolerated (Garcia-Sicilia et al., 2010).

*HPV vaccine in pregnancy.* In the absence of well-controlled studies in pregnant women, vaccination with HPV vaccine is not recommended in pregnancy as a precautionary measure. However, some data is available because pregnant women have been enrolled in phase III clinical trials with known pregnancy outcomes and through the establishment of pregnancy registers. In a combined analysis of pregnancy outcomes for women aged up to 45 years, the administration of Quadrivalent human papillomavirus vaccine to women who became pregnant during the phase III clinical trials did not appear to negatively affect pregnancy outcomes (Garland et al., 2009). A pooled analysis of two randomized controlled trials on the risk of miscarriage with Bivalent vaccine provided no evidence overall for an association between HPV vaccination and risk of miscarriage. Of 517 reports of pregnancies enrolled on a register, rates of spontaneous abortions and major birth defects were not greater than those in the unexposed population (Dana et al., 2009). An analysis of phase III trials and post-marketing data identifying reports of 90 pregnancies within 30 days of vaccination showed no increased risk of spontaneous abortion, fetal malformations, or adverse pregnancy outcomes in the general population (Forinash AB et al., 2011)

*Syncope in adolescent girls.* Post-marketing surveillance has documented a number of cases of syncope in adolescent girls (CDC, 2008). Possibly the rate of syncope is higher when the HPV vaccine is delivered as part of a school programme and vaccine providers should have measures in place to prevent syncope and syncope-related injury from occurring (Bernard DM et al., 2011).



**Summary of mild and severe adverse events - Quadrivalent HPV vaccine**

Nature of Adverse event	Description	Rate/doses
Mild	<i>Local adverse events</i>	
	Injection site reaction	83 per 100
	Erythema and swelling	25 per 100
	Severe - injection site erythema and/or swelling > 2 inches in size and pain severe	5.7 per 100
	<i>Systemic adverse events:</i>	
	Pyrexia	13 per 100
	Urticaria	3 per 100
	Headache	26 per 100
Severe	Myalgia	2 per 100
	Arthralgia	1 per 100
	Gastrointestinal disorders	17 per 100
	Anaphylaxis	1.7 – 2.6 per 10 <sup>6</sup>

Source: European Public Assessment Report (EMEA CHMP, 2006)

**Summary of mild and severe adverse events - Bivalent HPV vaccine**

Nature of Adverse event	Description	Rate/doses
Generally mild	<i>Local adverse events</i>	
	Injection site pain <sup>2</sup>	78 per 100
	Swelling <sup>2</sup>	26 per 100
	Redness	30 per 100
	<i>Systemic adverse events:</i>	
	Fatigue <sup>2</sup>	33 per 100
	Headache <sup>2</sup>	30 per 100
	Myalgia <sup>2</sup>	28 per 100
	Itching <sup>1</sup>	9 per 100
	Arthralgia <sup>2</sup>	10 per 100
	Gastrointestinal symptoms <sup>2</sup>	13 per 100
	Fever <sup>1</sup>	3 per 100
	Rash <sup>1</sup>	1 per 100
	Urticaria <sup>1</sup>	0.46 per 100

Source: Gasparini et al. (2011)<sup>1</sup>; European Public assessment report, EMEA CHMP (2006)<sup>2</sup>

This information sheet has been developed in close collaboration with the Global Advisory Committee on Vaccine Safety (GACVS). GACVS experts are independent and have declared no interests related to the expertise displayed in this product. Information displayed has been developed using primary sources such (Plotkin et al., 2008, Institute of Medicine of the National Academies 2011) and from data derived from a literature search on Pubmed in 2008 using key words "vaccine antigen", "Safety" and "adverse events". An independent expert provided a first draft which was reviewed by nominated experts and the GACVS. Data of different vaccines that may be found in this product should only be compared if there is indication that a comparative randomized controlled trial has been undertaken. The information sheets will be updated as new information may become available at the following web link: [http://www.who.int/vaccine\\_safety/vaccrates/en/index.html](http://www.who.int/vaccine_safety/vaccrates/en/index.html)



**World Health  
Organization**

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## References

- ADRAC Bulletin (2011) [http://portal.bpfk.gov.my/aeimages/File/MADRAC\\_BULLETIN\\_APRIL\\_2011.pdf](http://portal.bpfk.gov.my/aeimages/File/MADRAC_BULLETIN_APRIL_2011.pdf).
- Bernard DM, Cooper Robbins SC, McCaughey KJ, Scott CM, Skinner SR (2011). The domino effect: adolescent girls' response to human papillomavirus vaccination. *Med J Aust.*; Mar 21;194(6):297-300.
- Bohlke K, Davis RL, Marcy SM, Braun MM et al. (2003). Risk of anaphylaxis after vaccination of children and adolescents. *Pediatrics*;112: 815-820.
- Centers for Disease Control and Prevention (CDC). (2008). Syncope after vaccination--United States, January 2005-July 2007. *MMWR Morb Mortal Wkly Rep.* May 2;57(17):457-60. Dana A, Buchanan KM, Goss MA, Seminack MM, Shields KE, Korn S, Cunningham ML, Haupt RM. Pregnancy outcomes from the pregnancy registry of a human papillomavirus type 6/11/16/18 vaccine. *Obstet Gynecol.* 2009 Dec;114(6):1170-8.
- Commission on Human Medicines (2010). <http://www.mhra.gov.uk/home/groups/pl-p/documents/websitesresources/con096797.pdf> (last visited: Sep 2010).
- Dana A; Buchanan KM et al. (2010). Pregnancy Outcomes From the Pregnancy Registry of a Human Papillomavirus Type 6/11/16/18 Vaccine. *Obstetrical & Gynecological Survey*: March - Volume 65 - Issue 3 - pp 169-170
- Descamps D, Hardt K, Spiessens B, et al. (2009). Safety of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine for cervical cancer prevention: a pooled analysis of 11 clinical trials. *Hum Vaccin*;5:332-40.
- Einstein MH, Baron M, Levin MJ, Chatterjee A, Edwards RP, et al. for the HPV-010 Study Group (2009). Comparison of the immunogenicity and safety of Cervarix™ and Gardasil® human papillomavirus (HPV) cervical cancer vaccines in healthy women aged 18-45 years. *Human Vaccines*. October; 5(10): 705-19.
- Einstein MH, Baron M, Levin MJ, Chatterjee A, Fox B, Scholar S, Rosen J, Chakhtoura N, Meric D, Dessy FJ, Datta SK, Descamps D, Dubin G (2011). Comparative immunogenicity and safety of human papillomavirus (HPV)-16/18 vaccine and HPV-6/11/16/18 vaccine: Follow-up from Months 12-24 in a Phase III randomized study of healthy women aged 18-45 years. *Hum Vaccin.* Dec; 7(12):1343-58. Epub 2011 Dec 1.
- EMA CHMP (2006). European Public Assessment Report. [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR\\_-\\_Scientific\\_Discussion/human/000703/WC500021140.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Scientific_Discussion/human/000703/WC500021140.pdf), p. 29 ff.
- EMA CHMP (2007). European Public Assessment Report. [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR\\_-\\_Scientific\\_Discussion/human/000721/WC500024636.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Scientific_Discussion/human/000721/WC500024636.pdf).
- Forinash AB, Yancey AM, Pitlick JM, Myles TD (2011). Safety of the HPV Bivalent and Quadrivalent Vaccines During Pregnancy (February). *Ann Pharmacother.* 2011 Feb 1. [Epub ahead of print].
- Garcia-Sicilia J, Schwarz TF, Carmona A et al. (2010). Immunogenicity and safety of human papillomavirus-16/18 AS04-adjuvanted cervical cancer vaccine coadministered with combined diphtheria-tetanus-acellular pertussis-inactivated poliovirus vaccine to girls and young women. *J Adolesc Health.*, 46(2):142-51.
- Garland SM, Ault KA, Gall SA, et al. (2009). Pregnancy and infant outcomes in the clinical trials of a human papillomavirus type 6/11/16/18 vaccine: a combined analysis of five randomized controlled trials. *Obstet Gynecol*;114:1179-88.
- Gasparini R, Bonanni P, Levi M et al. (2011). Safety and tolerability of Bivalent HPV vaccine: an Italian post-licensure study. *Hum Vaccin.* 2011 Jan-Feb;7 Suppl:136-46. Epub.
- Gee J, Naleway A, Shui I et al. (2011). Monitoring the safety of Quadrivalent human papillomavirus vaccine: findings from the Vaccine Safety Datalink. *Vaccine.* 2011 Oct 26;29(46):8279-84. Epub.
- Paavonen J, Jenkins D, Bosch FX, Naud P et al. (2007). HPV PATRICIA study group. Efficacy of a prophylactic adjuvanted Bivalent L1 virus-like-particle vaccine against infection with human papillomavirus types 16 and 18 in young women: an interim analysis of a phase III double-blind, randomized controlled trial. *Lancet*; 369(9580):2161-70.
- Pedersen C, Petaja T, Strauss G, Rumke HC, Poder A, Richardus JH, Spiessens B, Descamps D, Hardt K, Lehtinen M, Dubin G (2007). HPV Vaccine Adolescent Study Investigators Network. Immunization of early adolescent females with human papillomavirus type 16 and 18 L1 virus-like particle vaccine containing AS04 adjuvant. *J Adolesc Health*; 40(6):564-71.
- Plotkin S, Orenstein W, Offit P., eds. (2008). *Vaccines*. 5th ed. Philadelphia: Saunders/Elsevier.
- Rüggeberg J, Gold M, Bayas MJ et al. (2007). The Brighton Collaboration Anaphylaxis Working Group. Anaphylaxis: Case definition and guidelines for data collection, analysis, and presentation of immunization safety data. *Vaccine*; 25: 5675-5684.
- HPV Gardasil and GBS (2008). <http://www.cdc.gov/vaccines/vpd-vac/hpv/downloads/hpv-gardasil-gbs.pdf> (Accessed 10/1/2008).
- Therapeutic Goods Administration (2008). Advice from the Therapeutic Goods Administration. HPV (Gardasil) <http://www.tga.gov.au/alerts/medicines/gardasil.htm> (Accessed 10/1/2008).
- Institute of Medicine of the National Academies (2011). *Adverse Effects of Vaccines: Evidence and Causality*. The National Academies Press.
- Markowitz LE, Dunne EF, Saraiya M, Lawson HW, Chesson H, Unger ER (2007). Recommendations of the Advisory Committee on Immunization Practices (ACIP). Quadrivalent Human Papillomavirus Vaccine. <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5602a1.htm> (visited 13 April 2012).
- Reisinger KS, Block SL, Collins-Ogle M et al. (2010). Safety, tolerability, and immunogenicity of gardasil given concomitantly with Menactra and Adacel. *Pediatrics*;125(6):1142-51. Epub 2010 May 3.
- Slade BA, Leidel L, Vellozzi C, et al. (2009). Postlicensure safety surveillance for Quadrivalent human papillomavirus recombinant vaccine. *JAMA*; 302(7):750-7.
- Therapeutic Goods Administration. (2010). <http://www.tga.gov.au/safety/alerts-medicine-gardasil-070624.htm> (last accessed June 2010).
- VAERS (2011) <http://www.cdc.gov/vaccinesafety/vaccines/hpv/gardasil.html> (last accessed 2011).
- van Klooster TM, Kemmeren JM, van der Maas NA, de Melker HE (2011). Reported adverse events in girls aged 13-16 years after vaccination with the human papillomavirus (HPV)-16/18 vaccine in the Netherlands. *Vaccine*. 2011 Jun 20;29(28):4601-7. Epub.
- Wacholder S, Chen BE, Wilcox A et al. (2010). Risk of miscarriage with Bivalent vaccine against human papillomavirus (HPV) types 16 and 18: pooled analysis of two randomized controlled trials. *BMJ*;340:c712. doi: 10.1136/bmj.c712.



## ANNEX 5. SAMPLE AEFI REPORTING FORM

## REPORTING FORM FOR ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

<p><b>*Patient name:</b></p> <p><b>*Patient's full Address:</b></p> <p>Telephone:</p> <p>Sex: <input type="checkbox"/> M <input type="checkbox"/> F</p> <p><b>*Date of birth (DD/MM/YYYY):</b> ___ / ___ / _____</p> <p>OR Age at onset : <input type="checkbox"/> Years <input type="checkbox"/> Months <input type="checkbox"/> Days</p> <p>OR Age Group: <input type="checkbox"/> &lt; 1 Year <input type="checkbox"/> 1 to 5 Years <input type="checkbox"/> &gt; 5 Years</p>	<p><b>*Reporter's Name:</b></p> <p>Institution / Designation, Department &amp; address:</p> <p>Telephone &amp; e-mail:</p>
--	--

**Health facility (or vaccination centre) name:**

<b>*Name of Vaccines Received</b>	<b>*Date of vaccination</b>	<b>*Time of vaccination</b>	Dose (e. g. 1 <sup>st</sup> , 2 <sup>nd</sup> , etc.)	<b>*Batch/ Lot number</b>	Expiry date

**\*Adverse event (s):**

- Severe local reaction     >3 days     beyond nearest joint  
 Seizures                     febrile     afebrile  
 Abscess  
 Sepsis  
 Encephalopathy  
 Toxic shock syndrome  
 Thrombocytopenia  
 Anaphylaxis  
 Fever ≥38°C  
 Other (specify) .....

Describe AEFI (Signs and symptoms):

Date &amp; Time AEFI started (DD/MM/YYYY):

\_\_\_ / \_\_\_ / \_\_\_\_\_       Hr  MinWas the patient hospitalized?     Yes  No

Date patient notified event to health system (DD/MM/YYYY):

\_\_\_ / \_\_\_ / \_\_\_\_\_

**\*Outcome:**
 Recovering     Recovered     Recovered with sequelae     Not Recovered     Unknown

 Died If died, date of death (DD/MM/YYYY): \_\_\_ / \_\_\_ / \_\_\_\_\_
Autopsy done:     Yes     No     Unknown

Past medical history (including history of similar reaction or other allergies), concomitant medication and other relevant information (e.g. other cases). Use *additional sheet if needed* :

**First Decision making level to complete:**Investigation needed:     Yes     No

If yes, date investigation planned (DD/MM/YYYY):

\_\_\_ / \_\_\_ / \_\_\_\_\_

**National level to complete:**

Date report received at national level (DD/MM/YYYY):

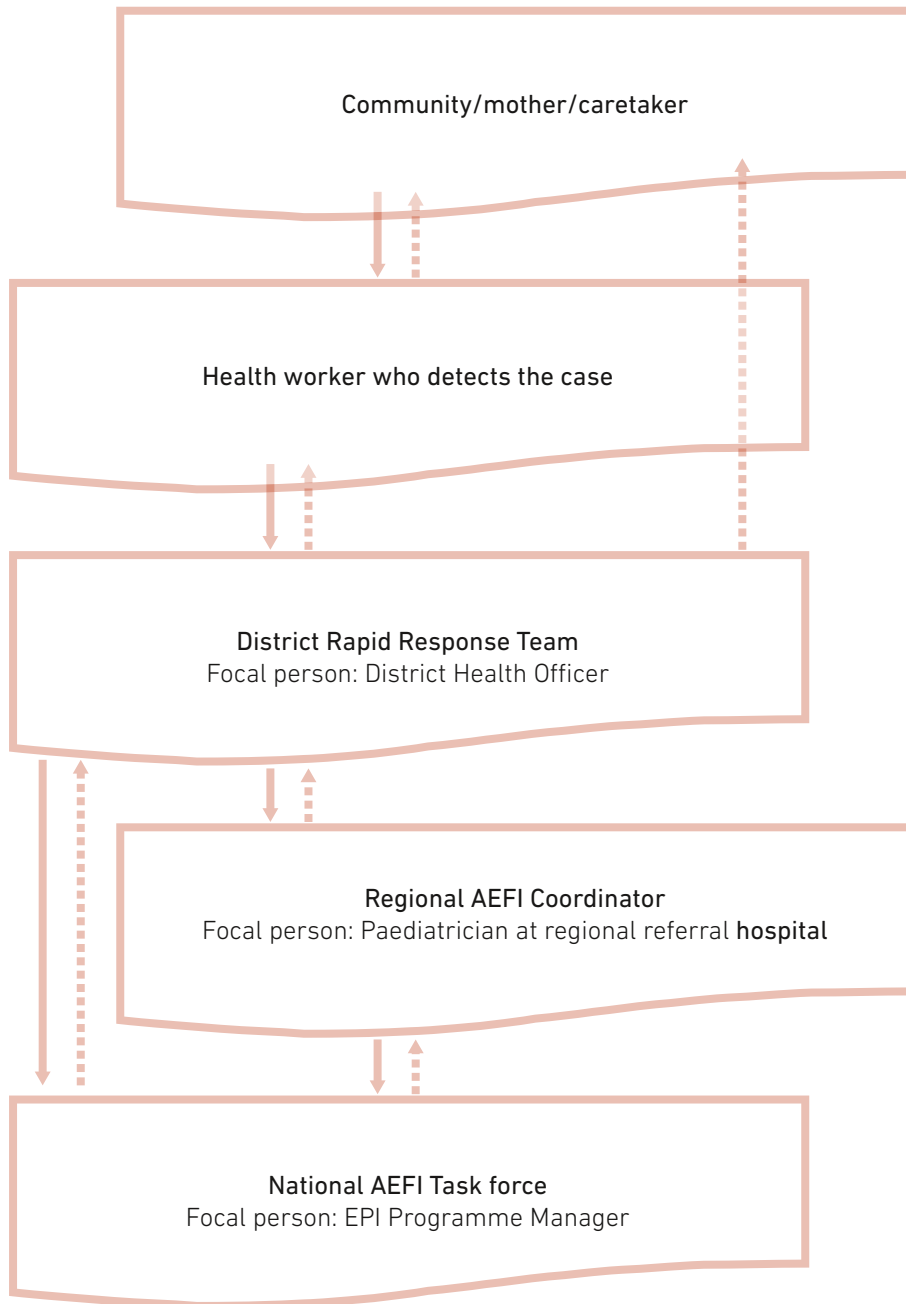
\_\_\_ / \_\_\_ / \_\_\_\_\_

 AEFI worldwide unique  
 ID :
   
 .....

Comments:

\*compulsory field

EXAMPLE OF GENERIC REPORTING FLOW FOR REPORTING AEFI



# ANNEX 6. AID MEMOIRE FOR AEFI INVESTIGATION AND SAMPLE AEFI INVESTIGATION FORM



WORLD HEALTH ORGANIZATION

## AEFI Investigation

### AIDE MEMOIRE

An **adverse event following immunization (AEFI)** is a medical incident that takes place after an immunization, causes concern and is believed to be caused by the immunization. Programmes providing immunization services should include a **system for AEFI detection and reporting, investigation and management, data analysis, corrective action, relevant communication and evaluation of the system.**

The ultimate **goal** of an investigation is to determine whether the vaccine or immunization process is responsible for the reported event(s) or to find another and correct it if possible, and reassure the public.

There are 4 possible causes of AEFI:

**Vaccine reaction:** event caused by some component of the vaccine – the active component of the vaccine itself, the preservative, the stabilizer or other. The majority of vaccine reactions are “common” and expected, mild, settle without treatment and have no long-term consequences. More serious reactions are very rare – usually of a fairly predictable (albeit extremely low) frequency;

**Programme error:** event caused by error in vaccine preparation, handling or administration;

**Coincidence:** event where something happens after the immunization but is not caused by the vaccine or the programme; and

**Injection reaction:** event arising from anxiety about the injection (needle).

The **purposes of investigating AEFI** cases are:

- 1) to confirm a reported diagnosis of AEFI and clarify the details and outcome;
- 2) to determine whether unimmunized persons are experiencing the same medical event(s);
- 3) to investigate the link between the vaccine given and the AEFI ;
- 4) to determine the contribution of operational aspects of the programme to the reported AEFI;
- 5) to determine whether a reported event was isolated or part of a cluster;
- 6) to determine the cause of the AEFI so as to provide the best intervention/medical care and take any further action deemed necessary.

In most cases, a preliminary **investigation** of an AEFI can be made by the health worker who detected the case, e.g. a health centre staff member or a nurse or physician in a hospital.

**Serious AEFI cases** or **AEFI clusters** should be investigated immediately with involvement from central levels including epidemiological and/or clinical expertise. A cluster of AEFIs can be defined as two or more cases of the same adverse event related in time, place or vaccine administered.

**Inadequate planning or response** may lead to a crisis with loss of confidence in the vaccination service. It is essential that programme managers:

- 1) **anticipate** the crisis and be prepared to deal with it when it occurs;
- 2) **verify** the facts of any event before making any public statement;
- 3) **are familiar with a plan** for reacting to any crisis should it happen. If no plan exists programme managers should develop one;
- 4) **be well informed** so that appropriate national and regional managers can be rapidly briefed to take charge and deal with political and media enquiries.



### Checklist

#### 1. Be prepared

- Read the resource documents on reporting, management and investigation of AEFIs.
- Develop standards: case definitions for reportable AEFIs, use of reporting forms and investigation procedures.
- Designate and train staff to conduct an AEFI investigation using the investigation form.
- Train staff on how to collect specimens.
- Establish procedure, criteria and designated person for notifying WHO and UNICEF (if UN-supplied vaccine) or other relevant party depending on procurement mechanism
- Establish a National Technical Advisory Committee with representation from major medical organizations
- Identify a spokesperson for public communications.

#### 2. Receiving a report

- Ensure immediate reporting of most serious events and rapid attention to reports received
- Verify the information in the report and classify and assess the AEFI using established case definitions. Decide whether it needs further investigating.
- If investigation is warranted, travel to the location of the AEFI, or delegate responsibility to another trained person

#### 3. Investigate and collect data

- Ask about the patient
- Ask about the vaccine and other drugs potentially received
- Ask about other vaccinees
- Ask about immunization services
- Observe the service in action
- Ask about cases in unvaccinated persons
- Establish a more specific case definition if needed
- Formulate a hypothesis as to what caused the AEFI

#### Collect specimens if appropriate:

- from the patient
- the vaccine (and diluent if applicable)
- the syringes and needles

#### 4. Dispatch specimens to appropriate testing facility (laboratory, regulatory authority, etc.)

#### 5. Analyze the data

- Review epidemiological, clinical, and laboratory findings
- Summarize and report findings

#### 6. Take action

- Communicate with health staff
- Communicate findings and action to the parents and public
- Correct problem (based on the cause) by improving training, supervision, and/or distribution of vaccines/injection equipment
- Replace vaccines if indicated

**Key data to be collected**

- 1) **Data on each patient**
  - demographic data about patient, including a unique case number, age, sex, place of residence, family history;
  - history of patient's present illness - symptoms and when each appeared and its duration, treatment, outcome, diagnosis;
  - history of patient's past illnesses e.g., reactions to previous vaccine doses, drug allergies;
  - pre-existing disorders, current medications;
  - immunization history - vaccine, number of doses received, date, and place of last immunization or immunizations, mode and site of administration;
  - laboratory results about blood, stool, or other samples, if appropriate and available
  - full autopsy report with toxicological screening and histopathological analysis
  - look for common environmental exposures between patients.
- 2) **Data about the vaccine(s) (and diluent if applicable) administered to the patient**
  - Lot number(s)
  - Expiry date(s)
  - Manufacturer(s)
  - Vaccine storage
  - Identify where the vaccine(s) was distributed
  - Whether other children were immunized with same lot or same vial at same session and elsewhere
  - Results of procedures to control vaccine quality
  - Laboratory test results about vaccine, if appropriate.
- 3) **Programme-related data.**
  - Common practices in storing and handling vaccines, and vaccine administration in the health centre in which the suspected immunization (or immunizations) were given. This may help identify products mistakenly used instead of vaccine or diluent
- 4) **Background data**
  - Establish if cases have been reported from elsewhere and actively look for additional cases among other vaccinees and at large in the community

**Role of the district/regional manager**

- 1) **Training**  
Staff should be trained in diagnosing, treating and reporting of AEFIs, and differentiating between mild, non-significant reactions and more serious events.
- 2) **Supervision**  
Non-serious AEFIs (e.g. abscesses) reported by peripheral health workers should be reviewed with training during site visits.
- 3) **Investigation and collection of data**  
Following a report of a serious AEFI, the manager should be responsible for investigation, collection and reporting of data. This may be under the overall supervision of a national team.
- 4) **Communication**  
The manager or designated person should set up the means for continuous communication between health workers and the community, directly and through the media. The public should be informed frequently about what is being done during an investigation and reassured where necessary.
- 5) **Correction of the problem**  
If an AEFI was caused by programme error the actions to be taken will probably include one or more of the following:
  - **Logistics**  
Improving logistics will be the appropriate response if programme errors can be traced to the lack of appropriate supplies or equipment, or to a failure in the cold chain.
  - **Training**  
Solving operational problems through training will deal with lack of skills and knowledge and with poor attitude.
  - **Supervision**  
Regular supervision and intensified when needed e.g., problems detected in reporting or programmatic errors identified.

**Did the vaccine or its delivery cause the reactions?**

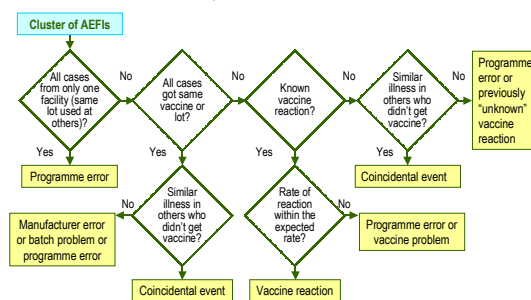
It will be necessary to determine if there is a causal association between the vaccine and the adverse event. In each case the following should be considered:

- Consistency of findings** – are all reported AEFIs the same?
- Temporal sequence** – confirm that the symptoms of AEFI occurred only after, not before, the vaccine was given and if the vaccine-event interval is compatible with a vaccine reaction
- Biological plausibility** – does the medical event seem plausibly due to an effect of the vaccine or other concomitant or preceding conditions?
- Previously known reaction** – check if this type of reaction is known to be related to the vaccine and with which frequency
- Specificity and strength of association** – establish if the same events are being reported in unvaccinated persons and if so, how often and if the cluster is limited to one health center or not
- Concomitant or preceding conditions**

AEFI evaluation requires a 2 by 2 table of exposures and outcomes and data should be collected in order to more fully complete the table and calculate a risk of event from receipt of the vaccine i.e.  $(a/a+c)/(b/b+d)$ . Cell a represents case reports only

	Possible Adverse Event	No Adverse Event
Vaccinated	a	c
Unvaccinated	b	d

**Suggested steps for the identification of the most likely cause of a cluster of AEFIs**



**Words of advice**

- The investigation should start within 24 hours of notification
- There is seldom need to test the vaccine unless clearly indicated by the epidemiologic investigation, but cold chain should be maintained
- A national committee can be very helpful in reviewing the outcome of the investigation and communication of findings
- Access medical files
- Rule out alternative aetiologies than the vaccination. The fact that an adverse event of the same nature has been previously related to a particular vaccine does not always mean that the case under investigation is also related to the vaccine
- Have direct discussions with the patients or parents if possible

Additional information on the definitions, monitoring, management and investigation of AEFIs can be found on the World-Wide Web at [www.who.int/immunization\\_safety/en](http://www.who.int/immunization_safety/en)

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**AEFI INVESTIGATION FORM**

(Only for Serious Adverse Events Following Immunization – Death / Disability / Hospitalization / Cluster)

Section A Basic details					
Province/State	District	Case ID			
Place of vaccination (✓): <input type="checkbox"/> Govt. health facility <input type="checkbox"/> Private health facility <input type="checkbox"/> Other (specify) _____					
Vaccination in (✓): <input type="checkbox"/> Campaign <input type="checkbox"/> Routine <input type="checkbox"/> Other (specify) _____					
Address of vaccination site:					
Name of Reporting Officer:			Date of investigation: ___ / ___ / ___		
Designation / Position:			Date of filling this form: ___ / ___ / ___		
Telephone # landline (with code):			This report is: <input type="checkbox"/> First <input type="checkbox"/> Interim <input type="checkbox"/> Final		
Mobile:			e-mail:		
Patient Name <span style="float: right;">Sex: <input type="checkbox"/> M <input type="checkbox"/> F</span>					
<small>(use a separate form for each case in a cluster)</small>					
Date of birth (DD/MM/YYYY): ___ / ___ / ___					
OR Age at onset: ___ years ___ months ___ days OR Age group: <input type="checkbox"/> < 1 year <input type="checkbox"/> 1–5 years <input type="checkbox"/> > 5 years					
Patient's full address with landmarks (Street name, house number, locality, phone number etc.):					
Name of vaccines/diluent received by patient	Date of vaccination	Time of vaccination	Dose (e.g. 1 <sup>st</sup> , 2 <sup>nd</sup> , etc.)	Batch/Lot number	Expiry date
				Vaccine	Vaccine
				Diluent	Diluent
				Vaccine	Vaccine
				Diluent	Diluent
				Vaccine	Vaccine
				Diluent	Diluent
				Vaccine	Vaccine
				Diluent	Diluent
				Vaccine	Vaccine
				Diluent	Diluent
Type of site (✓) <input type="checkbox"/> Fixed <input type="checkbox"/> Mobile <input type="checkbox"/> Outreach <input type="checkbox"/> Other _____					
Date of first/key symptom (DD/MM/YYYY): ___ / ___ / ___ Time of first symptom (hh/mm): ___ / ___					
Date of hospitalization (DD/MM/YYYY): ___ / ___ / ___					
Date first reported to the health authority (DD/MM/YYYY): ___ / ___ / ___					
Status on the date of investigation (✓): <input type="checkbox"/> Died <input type="checkbox"/> Disabled <input type="checkbox"/> Recovering <input type="checkbox"/> Recovered completely <input type="checkbox"/> Unknown					
If died, date and time of death (DD/MM/YYYY): ___ / ___ / ___ (hh/mm): ___ / ___					
Autopsy done? (✓) <input type="checkbox"/> Yes (date) ___ / ___ / ___ <input type="checkbox"/> No <input type="checkbox"/> Planned on (date) ___ / ___ / ___ Time ___					
Attach report (if available)					

Section B Relevant patient information prior to immunization		
Criteria	Finding	Remarks (if yes provide details)
Past history of similar event	Yes / No / Unkn	
Adverse event after previous vaccination(s)	Yes / No / Unkn	
History of allergy to vaccine, drug or food	Yes / No / Unkn	
Pre-existing illness (30 days) / congenital disorder	Yes / No / Unkn	
History of hospitalization in last 30 days, with cause	Yes / No / Unkn	
Patient currently on concomitant medication? (If yes, name the drug, indication, doses & treatment dates)	Yes / No / Unkn	
Family history of any disease (relevant to AEFI) or allergy	Yes / No / Unkn	
For adult women		
• Currently pregnant? Yes (weeks) _____ / No / Unknown		
• Currently breastfeeding? Yes / No		
For infants		
The birth was <input type="checkbox"/> full-term <input type="checkbox"/> pre-term <input type="checkbox"/> post-term.		Birth weight:
Delivery procedure was <input type="checkbox"/> Normal <input type="checkbox"/> Caesarean <input type="checkbox"/> Assisted (forceps, vacuum etc.) <input type="checkbox"/> with complication (specify)		

Name \_\_\_\_\_ Case ID Number \_\_\_\_\_ AEFI Investigation Page 2/4

Section C Details of first examination** of serious AEFI case		
Source of information (✓ all that apply): <input type="checkbox"/> Examination by the investigator <input type="checkbox"/> Documents <input type="checkbox"/> Verbal autopsy <input type="checkbox"/> Other _____ If from verbal autopsy, please mention source _____		
Name of the person who first examined/treated the patient: _____ Name of other persons treating the patient: _____ Other sources who provided information (specify): _____		
Signs and symptoms in chronological order from the time of vaccination:   		
Name and contact information of person completing these clinical details:	Designation:	Date/time
<p><b>**Instructions – Attach copies of ALL available documents (including case sheet, discharge summary, case notes, laboratory reports and autopsy reports) and then complete additional information NOT AVAILABLE in existing documents, i.e.</b></p> <ul style="list-style-type: none"> <li>• <b><i>If patient has received medical care</i></b> – attach copies of all available documents (including case sheet, discharge summary, laboratory reports and autopsy reports, if available) <u>and write only the information that is not available in the attached documents</u> below</li> <li>• <b><i>If patient has not received medical care</i></b> – obtain history, examine the patient and write down your findings below (add additional sheets if necessary)</li> </ul>		
<p><b>Provisional / Final diagnosis:</b></p>		

# ANNEX 7. SAMPLE HPV VACCINE REGISTER (INTEGRATED WITH OTHER VACCINES)

Region: \_\_\_\_\_ District: \_\_\_\_\_ Health Facility: \_\_\_\_\_

No.	IDENTIFICATION			RESIDENCE			HPV VACCINATION			Td VACCINATION			Comments	
	ID	Name	Date of Birth	Sex M/F	Prov.	District	Address	Telephone	Females 9 - 14 years	Adolescents 9 - 14 years	Dose 1 (DATE)	Dose 2 (DATE)		Dose 3 (DATE)
									Dose 1 (DATE)	Dose 2 (DATE)	Dose 3 (DATE)			

\*Please refer to WHO position paper on Tetanus vaccines for recommended schedules: [http://www.who.int/immunization/wer812tetanus\\_May06\\_position\\_paper.pdf](http://www.who.int/immunization/wer812tetanus_May06_position_paper.pdf)

## ANNEX 8. SAMPLE TALLY SHEET

Sample tally sheet to record number of HPV doses given on single vaccination day

Date: \_\_\_/\_\_\_/\_\_\_ Region: \_\_\_\_\_ District: \_\_\_\_\_ Health Facility: \_\_\_\_\_

Service Delivery Strategy (circle one): fixed/outreach/school. Location: \_\_\_\_\_


If school, grade: \_\_\_\_\_ Total number of eligible girls in the class: \_\_\_\_\_

Girls	HPV first dose (HPV1)	Total	HPV second dose (HPV2)	Total	Comments
9 years					
10 years					
11 years					
12 years					
13 years					
14 years					
15 or more years					
Unknown age					



## ANNEX 9. SAMPLE VACCINATION CARD

Sample vaccination card from South Africa, which includes parental consent and background information on the HPV vaccine.

 <p>Basic Education Health</p> <p>Human Papillomavirus (HPV) Vaccination Card</p> <p>Keep this card in a safe place. Bring this card along for the next dose.</p>	<p><b>Parent please complete and return to school</b></p> <p>ID. No. _____</p> <p>Name: _____</p> <p>Surname: _____</p> <p>Date of birth: _____</p> <p>Name of School: _____</p> <p>Grade: _____ Date: _____</p> <p>Name of parent/guardian _____</p> <p>_____ hereby grant permission for my daughter _____ (Name of daughter) to receive the HPV vaccination.</p> <p>_____ Signature Date: _____</p>	<table border="1"> <tr> <td>Parent please complete</td> <td>Y/N</td> </tr> <tr> <td>Allergic to any vaccine</td> <td></td> </tr> <tr> <td>Severe illness in the last 7 days</td> <td></td> </tr> <tr> <td colspan="2">Any other medical condition: _____</td> </tr> </table> <p>For official use only</p> <table border="1"> <tr> <td>Signature of Vaccinator</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Date</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Batch no.</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Dose</td> <td>HPV 1</td> <td>HPV 2</td> <td></td> </tr> </table>	Parent please complete	Y/N	Allergic to any vaccine		Severe illness in the last 7 days		Any other medical condition: _____		Signature of Vaccinator				Date				Batch no.				Dose	HPV 1	HPV 2		<p><b>Why HPV Vaccine?</b></p> <p><b>Cervical cancer</b></p> <ul style="list-style-type: none"> <li>➤ HPV is a viral infection that can cause cervical cancer</li> </ul> <p><b>HPV vaccine</b></p> <ul style="list-style-type: none"> <li>➤ Reduces your chances of developing cervical cancer</li> </ul> <p><b>Who gets the HPV vaccine?</b></p> <ul style="list-style-type: none"> <li>➤ Given to all girls in Grade 4 that are over 9 years</li> </ul> <p><b>Who should not get vaccinated?</b></p> <ul style="list-style-type: none"> <li>➤ Girls under 9 years</li> <li>➤ Girls who had a severe illness recently or are very ill now</li> </ul> <p><b>How is it given?</b></p> <ul style="list-style-type: none"> <li>➤ Injection in 2 doses</li> <li>➤ Second dose given 6 months after first dose</li> </ul> <table border="1"> <tr> <td colspan="2">For official use only</td> </tr> <tr> <td colspan="2">Date of Next Vaccine</td> </tr> <tr> <td></td> <td>HPV 2</td> </tr> <tr> <td></td> <td></td> </tr> </table>	For official use only		Date of Next Vaccine			HPV 2		
	Parent please complete	Y/N																																	
Allergic to any vaccine																																			
Severe illness in the last 7 days																																			
Any other medical condition: _____																																			
Signature of Vaccinator																																			
Date																																			
Batch no.																																			
Dose	HPV 1	HPV 2																																	
For official use only																																			
Date of Next Vaccine																																			
	HPV 2																																		

# ANNEX 10. SAMPLE MONTHLY VACCINATION REPORT

## Monthly Report – Human Papillomavirus Vaccine

Date: \_\_\_/\_\_\_/\_\_\_ Region: \_\_\_\_\_ District: \_\_\_\_\_

Age/Strategy	Target Pop.	HPV first dose (HPV1)				HPV second dose (HPV2)			
		Fixed	Outreach	School	Total	Fixed	Outreach	School	Total
9 years									
10 years									
11 years									
12 years									
13 years									
14 years									
15 or more years									
Unknown age									
<b>Total</b>									

## ANNEX 11. FREQUENTLY ASKED QUESTIONS (FAQS)

### Why are HPV vaccines needed?

Certain human papillomavirus (HPV) types cause cancer, including: cervical, vulvar, vaginal, penile, and anal cancers. Certain HPV types also cause most cases of genital warts.

HPV is a common virus that is easily spread by skin-to-skin contact during sexual activity with another person. It is possible to have HPV without knowing it, so it is possible to unknowingly spread HPV to another person.

HPV vaccine is an important tool for prevention. These safe, effective vaccines are available to protect against HPV types 16 and 18 that cause approximately 70% of cervical cancers worldwide.

### How common are the health problems caused by HPV?

HPV is the main cause of cervical cancer, the 4th most common cancer in women in the world. Of the 266,000 women who die every year from cervical cancer, over 85% live in developing countries.

### What WHO prequalified HPV vaccines are currently available?

Two HPV vaccines are currently prequalified by WHO. As of 2016, HPV vaccine has been introduced into the national immunization program in more than 65 countries. These vaccines are Cervarix® (GlaxoSmithKline) and GARDASIL® or Silgard® (Merck & Co.).

In 2016, a third vaccine (9-valent, GARDASIL 9®) is being reviewed for WHO prequalification.

### How are the currently available HPV vaccines similar?

All vaccines are very effective against diseases caused by HPV types 16 and 18; HPV 16 and 18 cause most cervical cancers, as well as other HPV-associated cancers.

All vaccines have been shown to prevent cervical pre-cancers in women.

All vaccines are very safe.

All vaccines are non-infectious and cannot cause disease.

All vaccines are given as injections and require two doses.

### How are the HPV vaccines different?

The vaccines have different adjuvants—a substance that is added to the vaccine to increase the body's immune response.

Two of the vaccines (the quadrivalent and the 9-valent) protect against HPV types 6 and 11, the types that cause most genital warts in females and males.

### Who should get HPV vaccine?

The WHO recommended target population for HPV vaccination is girls who are 9-14 years old. The vaccines are not licenced for use in girls younger than 9 years of age.

### Why is HPV vaccine recommended at ages 9-14 years old?

For the HPV vaccine to work best, it is very important for preteens to get two doses long before any sexual activity with another person begins. It is possible to be infected with HPV the very first time that a person has sexual contact with another person. Also, the vaccine produces higher antibody levels when given at this age compared to older ages.

**What is the recommended schedule (or timing) of the two HPV doses (shots)?**

Two doses (shots) are recommended 6-12 months apart.

**What is the maximum interval between HPV doses? If a child received only one dose, and presents again 2 years later, should the series be continued?**

There no maximum interval between HPV vaccine doses, hence no need to restart the series. The child should be vaccinated and the vaccination recorded as the 2<sup>nd</sup> dose.

**What is the minimum interval between doses?**

HPV vaccine doses should be given at least 5 months apart. If the interval between doses is shorter than 5 months, then a third dose should be given at least 6 months after the first dose.

**Are the HPV vaccines safe and effective?**

Most national regulatory agencies, including the Food and Drug Administration in the U.S.A. and the European Medicines Agency, have licensed the vaccines and note them to be safe and effective. Both vaccines have been administered to millions of girls and women around the world without serious side effects. Common, mild side effects included pain where the injection was given, fever, headache, and nausea. As with all vaccines, the safety of these vaccines is monitored very carefully. Ongoing vaccine safety studies continue to show that HPV vaccines are safe.

**Can HPV vaccines treat HPV infections or cervical cancer?**

HPV vaccines will not treat or get rid of existing HPV infections. In addition, HPV vaccines do not treat or cure diseases (like cancer or warts) caused by an HPV infection that occurred before vaccination. It is important for adult women to still get cervical cancer screening even if they have completed the HPV vaccine series.

**How important is it to get HPV vaccine?**

The HPV vaccines are important tools to prevent cervical cancer caused by HPV types targeted by the vaccine.

**Should pregnant women be vaccinated?**

HPV vaccines are not recommended for use in pregnant women. However, studies have shown neither vaccine caused problems for babies born to women who got the HPV vaccine while they were pregnant. Receiving the HPV vaccine when pregnant is not a reason to consider ending a pregnancy. But, to be on the safe side until more is known, a pregnant woman should not get any doses of either HPV vaccine until her pregnancy is completed.

**What should a woman do if she realizes she received HPV vaccination while pregnant?**

If a woman realizes that she received HPV vaccine while pregnant, she should wait until after her pregnancy to finish the remaining HPV vaccine doses.

**Can women with HIV infection be vaccinated?**

Studies show that HPV vaccination is safe and immunogenic and does not cause problems for HIV-infected women who got the vaccine. HPV vaccine is not contraindicated in HIV-infected women. Girls 9-14 year old who are HIV positive, should however receive an additional dose (3 doses total) to be fully protected.

**Can females with physical disabilities be vaccinated?**

Yes. Physical handicap is not a contraindication for HPV vaccination.

### **Can boys get vaccinated?**

HPV vaccines are currently not recommended by WHO for administration to boys for prevention of cervical cancer because high vaccine coverage (>70%) in the primary target population of 9-14 year old girls is more cost-effective in reducing cervical cancer than including boys.

### **What should be done if boys are given the HPV vaccine in error?**

There is no harm for boys to receive HPV vaccine. If boys are accidentally given HPV vaccine this is a programmatic error and training/supervision should be undertaken to correct. For ethical reasons and to prevent the spread of rumours, the "mistake" should be explained to the boys and their parents/guardians (emphasizing that it is safe and in countries elsewhere e.g. Austria, Australia, and United States, boys are vaccinated with HPV). If the vaccine used was the quadrivalent or 9-valent (which protect against genital warts) then the 2nd dose should be offered to the boys. As the bivalent vaccine is not licensed for use in boys, a 2nd dose should not be offered.

### **Do people faint after getting HPV vaccines?**

People faint for many reasons. Some preteens and teen may faint after any medical procedure, including receiving vaccines. It is possible for falls and injuries to occur after fainting. Sitting or lying down for about 15 minutes after a vaccination can help prevent fainting and related injuries.





This document is intended for use by national immunization programme managers and immunization partners to inform the policy discussions and operational aspects for the introduction of HPV vaccine into national immunization programmes and to provide up-to-date references on the global policy, as well as the technical and strategic issues related to the introduction of HPV vaccine.

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